Complete Summary

GUIDELINE TITLE

Global strategy for asthma management and prevention.

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2005. 184 p. [1372 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2004. 182 p.

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Asthma

GUIDELINE CATEGORY

Diagnosis
Evaluation
Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Emergency Medicine
Family Practice
Internal Medicine
Nursing
Pediatrics
Preventive Medicine
Pulmonary Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians
Public Health Departments
Respiratory Care Practitioners

GUIDELINE OBJECTIVE(S)

- To facilitate the successful management of asthma; to prevent chronic disability and premature death due to asthma; and to facilitate productive and fulfilling lives for people with asthma
- To extend the relevance of and impact of the National Heart, Lung, and Blood Institute's (NHLBI) "International Consensus Report on Diagnosis and Management of Asthma," by adapting the recommendations for the clinical management of asthma in order to ensure their appropriateness throughout the global community
- To deliver information to public health officials about the costs of asthma, prevention activities, and education methods; so that they can develop asthma care services and programs responsive to the particular needs and circumstances of their countries
- To develop information, recommendations, and tools to assist health care professionals and public health officials in appreciating the magnitude of the asthma problem in their countries and in designing and delivering effective asthma management and prevention programs in their communities
- To identify areas for future research investigations
- To update and incorporate the many advances detailed in scientific publications from January 2004 through December 2004

TARGET POPULATION

Patients of all ages in countries throughout the world with asthma

INTERVENTIONS AND PRACTICES CONSIDERED

1. Identification of risk and contributing factors for asthma
2. Diagnosis of asthma, including history and measurements of symptoms; physical examination; and measurements of lung function (spirometry; peak expiratory flow; airway hyper-responsiveness)
3. Classification of asthma on the basis of etiology, severity, and pattern of airflow limitation
4. Prevention of asthma
5. A six-part asthma management program, including the following elements:
    - Educate patients to develop a partnership in asthma management
    - Assess and monitor asthma severity with both symptom reports and, as much as possible, measurements of lung function (using peak expiratory flow or peak expiratory flow information). Measurement of arterial blood gases is also considered, especially for patients in the emergency department
    - Avoid or control asthma triggers: controlling exposure to allergens, pollutants, and pharmacologic agents. Influenza vaccination and specific immunotherapy are also considered
    - Establish individual medication plans for long-term management:
        - Long-term preventive (controller) medications:
            - Corticosteroids
            - Sodium cromoglycate
            - Nedocromil
            - Sustained-release theophylline
            - Long-acting beta2-agonists
            - Ketotifen
            - Antileukotrienes
            - Anti-immune globulin E (IgE)
            - Second-generation antihistamines
            - Systemic steroid-sparing therapies
            - Allergen-specific immunotherapy
        - Quick-relief (reliever) medications:
            - Short-acting inhaled beta2-agonists
            - Systemic corticosteroids
            - Inhaled anticholinergics
            - Short-acting theophylline
            - Short-acting oral beta2-agonists
            - Epinephrine/adrenaline injection
        - Traditional methods of healing or
    - Establish plans for managing exacerbations: including assessment of the severity of the exacerbation, and:
        - Home management of exacerbations: action plan and treatment including bronchodilators and corticosteroids; and additional care (continued medications)
        - Hospital-based management of exacerbations: including assessment of the patient; treatment (including oxygen, a combination of oxygen and helium [heliox], beta2-agonists, epinephrine, additional bronchodilators, and corticosteroids); and considerations of other treatments

- Provide regular follow-up care

MAJOR OUTCOMES CONSIDERED

- Chronic, including nocturnal, symptoms
- Asthmatic episodes (acute exacerbations)
- Emergency room visits
- Activities, including exercise
- Lung function measurements (peak expiratory flow)
- Adverse effects from medicine
- Morbidity (including quality of life and hospital admissions) due to exacerbations and persistent symptoms
- Mortality due to asthma
- Socioeconomic factors (e.g., absence from school or work, restriction of physical activity, time spent caring for individual with asthma)

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The 2005 update includes the impact of publications from January 1 through December 2004.

The process included a Pub Med search using search fields established by the Committee: 1) asthma, All fields, All ages, only items with abstracts, Clinical Trial, Human, sorted by Authors; and 2) asthma AND systematic, All fields, All ages, only items with abstracts, Human, sorted by Author. In addition, publications in peer review journals not captured by Pub Med could be submitted to individual members of the Committee, providing an abstract and the full paper were submitted in (or translated into) English.

All members of the Committee received a summary of citations and all abstracts. Each abstract was assigned to 2 Committee members, although any member was offered the opportunity to provide an opinion on any abstract. Members evaluated the abstract or, up to her/his judgment, the full publication, by answering specific written questions from a short questionnaire, and indicated if the scientific data presented impacted on recommendations in the Global Initiative for Asthma (GINA) Workshop report.

NUMBER OF SOURCE DOCUMENTS

Between January 1 and December 31, 2004, 296 articles met the search criteria; 2 additional publications were brought to the attention of the committee. Of these, 25 papers were identified to have an impact on the Global Initiative for Asthma (GINA) workshop report that was posted on the Web site in October 2004

either by 1) confirming, that is, adding or replacing an existing references, or 2) modifying, that is, changing the text or introducing a concept that required a new recommendation to the report.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Members of the Executive Committee chose to assign levels of evidence to statements using the system developed by the National Heart, Lung, and Blood Institute (NHLBI).

Description of Levels of Evidence

A. Randomized controlled trials. Rich body of data.
   Definition: Evidence is from endpoints of well-designed randomized controlled trials that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B. Randomized controlled trials. Limited data.
   Definition: Evidence is from endpoints of intervention studies that include only a limited number of randomized controlled trials, post hoc or subgroup analysis of patients, or meta-analysis of randomized controlled trials. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C. Nonrandomized trials. Observational studies.
   Definition: Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D. Panel consensus judgment.
   Definition: This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was deemed insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The first draft of the updated document was discussed during a workshop cosponsored by the National Heart, Lung, and Blood Institute (NHBLI) and the World Health Organization (WHO) in Toronto, Canada in May, 2000 at the time of an annual American Thoracic Society meeting. Additional drafts of the chapters were prepared and reviewed by members of the Global Initiative for Asthma (GINA) Executive Committee in October, 2000, January, 2001 and May, 2001.

For the 2005 Update, the entire GINA Science Committee met on a regular basis to discuss each individual publication that was indicated to have an impact on asthma management and prevention by at least 1 member of the Committee, and to reach a consensus on the changes in the report. Disagreements were decided by vote.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

- Several studies in the United Kingdom have looked closely at the links between the process of clinical care and economic outcomes. One study showed that integrated primary and secondary care was cost effective. Another study found that nurse-led intervention to improve the diagnosis and treatment of childhood asthma in primary care led to a reduction in hospital care costs. It should be noted, however, that these positive outcomes tend to diminish over time, indicating a need to sustain the intensity of the intervention. Primary care of asthma by a trained asthma nurse may be associated with a favorable clinical outcome and, by implication, reduced health service costs. The cost of treating acute asthma attacks is far greater than the cost of providing preventive drug treatment.
- Economic evaluation of asthma self-management programs has shown them to be cost effective, largely because they reduce patients' use of health care resources. The cost-benefit ratios in published studies are between 1:2.5 and 1:7. However, further studies in this area are clearly needed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

In July 2001, the guideline document was sent for review to all authors, as well as individuals and medical societies interested in the management of asthma. The reviewers' comments were incorporated, as appropriate, into the final document by the Chair of the Global Initiative for Asthma Executive Committee and the Chair of the Global Initiative for Asthma (GINA) Scientific Committee in cooperation with members of the Expert Panel.

Prior to the release of the 2005 Update, the proposed modifications to the 2002 GINA Workshop Report were submitted to the GINA Executive Committee for approval.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Evidence grades (A-D) are defined and a list of abbreviations is provided at the end of the "Major Recommendations" field.

Summary of New Recommendations in the 2005 Update

The major modifications introduced in the management section in the 2005 update include (page numbers refer to the original guideline document):

- Pg 41--Menstruation might act as a contributing factor in the development of near fatal asthma episodes in patients with unstable asthma.
- Pg 99--Among inner city children with atopic asthma, an individualized, home-based, comprehensive environmental intervention was shown to reduce asthma morbidity.
- Page 102--Several new publications led to a revision of the paragraph on Vaccination:

  Patients with moderate to severe asthma should be advised to take an influenza vaccination every year or at least when vaccination of the general population is advised. However, routine influenza vaccination of children and adults with asthma does not appear to protect them from asthma exacerbations. Inactivated influenza vaccines are associated with few side effects, and are safe to administer to asthmatic adults and children over the age of 3 years, including those with severe asthma. There are data to suggest that intra-nasal vaccination may be associated with an increased incidence of asthma exacerbations in children under age 3.

- Pg 106--Patients with severe persistent asthma and impaired airway caliber seem to be protected from developing systemic adverse effects with high-dose fluticasone propionate therapy, as evaluated by basal and dynamic measures of hypothalamic-pituitary-adrenal axis activity.
- Pg 107--Figure 7-3.5, "Steroids and Osteoporosis," was added, along with several references.
- Pg 123--Even for administration of inhaled beta2-agonists during episodes of severe acute asthma, the nebulizer can be replaced by pressurized metered dose inhaler (MDI) with a spacer.
- Pg 129--One large study confirmed that low dose inhaled glucocorticosteroids are superior to sodium cromoglycate (5mg 4 times daily) in children age 1 to 3 years.

The committee also added seventeen references that provided confirmation of previous recommendations.

Overall Guideline Recommendations (2005 Update)

Diagnosis and Classification

Key Points

- Asthma is underdiagnosed throughout the world.
- Asthma can often be diagnosed on the basis of symptoms. However, measurements of lung function, and particularly the reversibility of lung function abnormalities, greatly enhance diagnostic confidence.
- Lung function measurements that are most helpful for the diagnosis of asthma (in patients over 5 years of age) include forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), peak expiratory flow (PEF), and airway hyperresponsiveness.
- Asthma severity is classified by the presence of clinical features before treatment is started and/or by the amount of daily medication required for optimal treatment.
- Measurements of allergic status add little to the diagnosis of asthma but can help in the identification of risk factors so that appropriate environmental control measures can be recommended.
- Special care should be given to diagnosing asthma in children, in individuals with recurrent cough, in the elderly, and in individuals exposed to occupational agents known to cause asthma.

Clinical Diagnosis

History and Measurements of Symptoms

A clinical diagnosis of asthma is often prompted by symptoms such as episodic breathlessness, wheezing, and chest tightness. Seasonal variability of symptoms and a positive family history of asthma and atopic disease are also helpful diagnostic guides.

The following questions are useful when considering a diagnosis of asthma:

- Has the patient had an attack or recurrent attacks of wheezing?
- Does the patient have a troublesome cough at night?
- Does the patient have a wheeze or cough after exercise?
- Does the patient have wheeze, chest tightness, or cough after exposure to airborne allergens or pollutants?
- Do the patient's colds "go to the chest" or take more than 10 days to clear up?
- Are symptoms improved by appropriate anti-asthma treatment?

Figure 5-2 titled "International Union Against Tuberculosis and Lung Disease (IUATLD) Asthma Questionnaire" in the original guideline document presents a questionnaire that has been used and validated for the diagnosis of asthma in epidemiological studies. Measurements of symptoms and lung function are important parameters for assessing the characteristics of the patient's asthma. Various symptom scores have been developed and validated in order to quantify asthma control and quality of life. Symptom scores should be adapted to the age and the cultural background of the patient.

Physical Examination

Because asthma symptoms are variable, the physical examination of the respiratory system may be normal. The most usual abnormal physical finding is wheezing on auscultation. However, some people with asthma may have normal auscultation but significant airflow limitation when measured objectively.

Clinical signs such as dyspnea, airflow limitation (wheeze), and hyperinflation are more likely to be present if patients are examined during symptomatic periods. During an exacerbation of asthma, contraction of airway smooth muscle, edema, and hypersecretion tend to close the smaller (noncartilaginous) airways. To compensate, the patient breathes at a higher lung volume to increase outward retraction of the airways, thereby helping to maintain their patency. Thus the more severe the airflow limitation, the greater the tendency for airway closure to occur, and the higher the lung volume must be to keep airways open. The combination of hyperinflation and advanced airflow limitation in an asthma exacerbation also markedly increases the work of breathing.

Although wheezing is the most typical physical finding in asthma, this sign may be absent in severe asthma exacerbations. However, patients in this state usually have other physical signs reflecting severity, such as cyanosis, drowsiness, difficulty speaking, tachycardia, hyperinflated chest, use of accessory muscles, and intercostal recession.

Measurements of Lung Function

Measurements of lung function, particularly the reversibility of lung function abnormalities, provide a direct assessment of airflow limitation. Measuring the variability in lung function provides an indirect assessment of airway hyperresponsiveness. However, although some relationship has been established between laboratory indices of airway hyperresponsiveness and PEF variability, they are not interchangeable. For example, PEF variability may respond rapidly to glucocorticosteroid treatment, whereas histamine or methacholine airway responsiveness improves over a slower time course. Nevertheless, measurements of airflow limitation, its reversibility (see Figure 1-5 titled "Dose-Response Relationship Between Constrictor Agonist and Decrease in an Index of Airway Caliber in Normal Subjects and People With Asthma" and Figure 1-7 titled "Typical Spirometric Tracings From a Normal Subject, a Subject With Asthma, and a Subject With Asthma After Using a Bronchodilator (bd)" in the original guideline document), and its variability (see Figure 1-6 titled "Characteristic PEF Chart of a Patient With Uncontrolled Asthma Showing Within- and Between-Day Variation and the Response of a Reduced Morning PEF to a Bronchodilator (bd)" in the original guideline document) are considered critical in establishing a clear diagnosis of asthma. These measurements underlie the new asthma management strategies advocated in established asthma guidelines. Measurement of lung function for diagnosing and monitoring asthma is analogous to measurement in other chronic diseases. For example, blood pressure measured with a sphygmomanometer is used for diagnosing and monitoring hypertension, and blood glucose measured with reagent strips or digital read-out meters is used for diagnosing and monitoring diabetes.

A wide range of different methods to assess the level of airflow limitation exists, but two methods have found widespread acceptance for use in patients over 5 years of age. These are the measurement of FEV_1 and its accompanying FVC, and the measurement of PEF.

Spirometry. Measurement of FEV_1 and FVC is undertaken during a forced expiratory maneuver using a spirometer. Recommendations for the standardization of spirometry have been published. The procedure is repeatable, but effort dependent; therefore, proper instructions on how to perform the forced expiratory maneuver must be given to patients, and the highest values of two or three recordings taken. The test begins to lose its reliability at values of FEV_1 less than 1 liter. Predicted values of FEV_1, FVC, and PEF based on age, gender, and height have been obtained from population studies, and although these are being continually revised, they form some useful bases against which to judge whether a given value is abnormal or not. It is important that predicted values of FEV_1, FVC, and PEF take into account ethnic characteristics and extremes of age. Because diseases other than those causing airflow limitation may result in reduced FEV_1, a useful assessment of airflow limitation can be obtained as the ratio of FEV_1 to FVC. In the normal lung, flow limitation on forced expiration results in FEV_1/FVC ratios of greater than 80 percent and in children possibly greater than 90 percent. Any values less than these are suggestive of airflow limitation.

Spirometry is helpful for the diagnosis of asthma, where at least a 12 percent improvement in FEV_1 either spontaneously, after inhalation of a bronchodilator, or in response to a trial of glucocorticosteroid therapy favors a diagnosis of asthma. Spirometry is also helpful for monitoring the activity of the asthma, although primarily in a clinic health care setting because the apparatus is cumbersome and moderately expensive. Small electronic spirometers have been developed for portable use, but expense is likely to limit their widespread acceptance. Nevertheless, spirometry recordings are helpful in diagnosing asthma and assessing its severity, and recordings at regular intervals (dependent upon the severity of the disease) assist in monitoring the long-term progress of asthma and its long-term response to therapeutic interventions. Spirometry, as opposed to PEF monitoring, is particularly helpful in assessing progress in patients with greatly compromised lung function (e.g., the elderly person with asthma and chronic obstructive pulmonary disease) because PEF measurements can be relatively well preserved in such patients in the presence of greatly reduced spirometric values.

PEF. An important aid in the diagnosis and subsequent treatment of asthma is the PEF meter. In some countries, PEF meters are becoming available on health service prescription. Recent versions of the PEF meter are relatively inexpensive (at least in affluent countries), portable, plastic, and ideal for patients to use in home settings for day-to-day objective monitoring of asthma.

PEF meters are useful in clinic and primary health care settings to help in the diagnosis of asthma, where at least a 15 percent improvement after inhalation of a bronchodilator or in response to a trial of glucocorticosteroid therapy favors a diagnosis of asthma. PEF meters are also useful for ongoing supervision of asthma if spirometry is impractical (see Figure 1-6 titled "Characteristic PEF Chart of a Patient With Uncontrolled Asthma Showing Within- and Between-Day Variation and the Response of a Reduced Morning PEF to a Bronchodilator (bd)" in the

original guideline document). Finally, regular home monitoring of PEF is sometimes useful because it can help patients detect early signs of asthma deterioration. Several studies have demonstrated that patients' symptom reports are unreliable indicators of airflow limitation. Poor perception of the severity of asthma on the part of the patient and health care professional has been cited as a major factor causing delay in treatment and thus may contribute to increased severity and mortality from asthma exacerbations. However, this is not the case with all patients. One study showed that symptoms preceded the onset of declines in lung function.

It is important to note that measurements of PEF do not always correlate with other measurements of lung function in asthma and are not necessarily interchangeable in evaluating asthma severity. For example, in children with asthma, PEF can be normal as airflow obstruction and gas trapping worsens. Therefore PEF can underestimate the degree of airflow obstruction. Also, in children, measurements of PEF do not always correlate with symptoms or other measures of disease severity. For these reasons, PEF measurements are ideally compared to the patient's own previous best measurements.

Careful instruction is required if patients are to reliably measure PEF because PEF measurements, like FEV_1 and FVC measurements, are effort dependent. A PEF meter may be used regularly throughout the day and over weeks and months to aid in the assessment of asthma severity and monitor the response to treatment. The severity of asthma is reflected not only in the level of baseline airflow limitation, but also in its variability, particularly across 24 hours (see Figure 1-6 titled "Characteristic PEF Chart of a Patient With Uncontrolled Asthma Showing Within- and Between-Day Variation and the Response of a Reduced Morning PEF to a Bronchodilator (bd)" in the original guideline document). Ideally PEF should be measured first thing in the morning when values are usually close to their lowest and last thing at night when values are usually at their highest.

One method of describing diurnal PEF variability is as the amplitude (the difference between the prebronchodilator morning value and the postbronchodilator value from the evening before), expressed as a percentage of the mean daily PEF value. Another method is the minimum morning prebronchodilator PEF over 1 week, expressed as a percent of the recent best (Min%Max) (see Figure 5-3 titled "A Simple Index of PEF Variation" in the original guideline document). This latter method has been suggested to be the best PEF index of airway lability because it requires only a once-daily reading, it correlates better than any other index with airway hyperresponsiveness, and the calculation is simple.

A diurnal variation in PEF of more than 20 percent is considered to be diagnostic of asthma, the magnitude of the variability being broadly proportional to disease severity (see Figure 1-6 titled "Characteristic PEF Chart of a Patient With Uncontrolled Asthma Showing Within- and Between-Day Variation and the Response of a Reduced Morning PEF to a Bronchodilator (bd)" in the original guideline document). However, it should be noted that in mild intermittent asthma or in severe intractable disease, variability in PEF may not be present or may be lost. In more severe asthma, diurnal variation and reversibility may not be a feature until after a trial of glucocorticosteroids. Even then, the more severe

intransigent forms of the disorder may take many weeks of treatment before reversibility becomes apparent.

By using a combination of regular symptom recording and PEF measurement, patients can be provided with treatment plans that are responsive to asthma severity, and the course of asthma can be effectively monitored. Furthermore, it is conceivable that a patient's adherence to treatment may be enhanced by observing objectively his/her responses to therapy.

Although long-term PEF monitoring for most patients with persistent asthma can be valuable and may be an ideal, this is not always possible for reasons of cost, cooperation, and availability of peak flow meters. However, short-term monitoring is particularly recommended for establishing a diagnosis, identifying possible environmental triggers, and evaluating changes in therapy. Long-term monitoring is particularly recommended for those patients with severe asthma, for those with poor perception of severity, and for those who have ever been hospitalized.

PEF measurement may be of use not only in establishing a diagnosis of asthma and assessing its severity but also in uncovering an occupational cause for asthma. When used in this way, PEF should be measured more frequently than twice daily and special attention paid to changes occurring inside and outside the workplace.

If, in the presence of infrequent symptoms, these tests fail to support a diagnosis of asthma, it is usually advisable to maintain surveillance with periodic reevaluation until the diagnostic situation becomes clearer. In these circumstances, the health care professional should take special consideration of the patient's family history, age, and asthma triggers before deciding on a diagnostic or therapeutic course of action. When there is doubt, a trial of treatment with short-acting beta2-agonists as needed and inhaled glucocorticosteroids is considered one of the surest ways of establishing a diagnosis of asthma, especially if combined with PEF monitoring. A clear knowledge of the degree of lung dysfunction (such as with daily measurements of PEF) over a period of time not only offers the opportunity for detecting environmentally related causes of the asthma but also provides the criteria for assessing asthma severity and environmental influences, and for observing the response to treatment.

The clinician must always feel confident that the diagnosis of asthma is fully established because the consequences for the patient are considerable and frequently lifelong. The requirements for diagnostic confirmation in patients presenting with severe symptoms and gross lung dysfunction differ from those for asymptomatic patients.

Airway hyperresponsiveness. For patients with symptoms consistent with asthma, but normal lung function, measurements of airway responsiveness to methacholine, histamine, or exercise challenge may help establish a diagnosis of asthma. These measurements are sensitive for a diagnosis of asthma, but have low specificity. This means that a negative test can be useful to exclude a diagnosis of persistent asthma, but a positive test does not always mean that a patient has asthma. This is because airway hyperresponsiveness has been described in patients with allergic rhinitis and in those with airflow limitation

caused by conditions other than asthma, such as cystic fibrosis, bronchiectasis, and chronic obstructive pulmonary disease.

Measuring Non-Invasive Markers of Airway Inflammation

The evaluation of airway inflammation associated with asthma may be undertaken by examining spontaneously produced or hypertonic saline-induced sputum for eosinophils and metachromatic cells. In addition, levels of exhaled nitric oxide (NO) or carbon monoxide (CO) have been suggested as noninvasive markers of airway inflammation in asthma. Levels of exhaled NO and CO are elevated in people with asthma (who are not taking inhaled glucocorticosteroids) compared to people without asthma, yet these findings are not specific for asthma. Neither sputum eosinophilia nor exhaled gases has yet been evaluated prospectively as an aid in asthma diagnosis. There is a need to develop further noninvasive discriminate measurements of airway inflammation.

Measurements of Allergic Status

The presence of an allergic component in asthma can be identified by skin testing or measurement of specific immunoglobulin E (IgE) in serum. While these tests add little to the diagnosis of asthma, they can help in identifying its risk factors or triggers so that appropriate environmental control measures can be recommended. Deliberate provocation of the airways with a suspected allergen or sensitizing agent may also be helpful in establishing causality, especially in the occupational setting, but is not routinely recommended, because it is not often useful in establishing a diagnosis and on the grounds of safety.

Skin tests with allergens represent the primary diagnostic tool in determining atopic status. Prick tests are the most commonly used for diagnostic purposes. Their characteristics--simplicity, rapidity of performance, low cost, and high sensitivity--explain their key position. However, when improperly performed, skin tests can lead to falsely positive or negative results. Measurement of specific IgE in serum does not surpass skin tests and is more expensive. The main limitation of methods to assess allergic status is that a positive test does not necessarily mean that the disease is allergic in nature, as some individuals have specific IgE antibodies without any symptoms. The relevant exposure and its relation to symptoms must be confirmed by the patient history. Measurement of total IgE in serum has no value as a diagnostic test for atopy.

Particularly Difficult Diagnostic Groups

In this section, emphasis is given to the difficult problems in diagnosing asthma in children, in the elderly, in relation to occupational exposure to risk factors, in seasonal asthma, and in cough variant asthma. For these patient groups measurements of airflow limitation and variability are extremely useful for establishing a diagnosis of asthma.

Childhood Asthma

Diagnosis of asthma in children can present a particularly difficult problem, largely because episodic wheezing and cough are among the most common symptoms

encountered in childhood illnesses, particularly in children under 3 years old. Although health care professionals are increasingly encouraged to make a positive diagnosis of asthma whenever recurrent wheezing, breathlessness, and cough occur (particularly if these symptoms occur at night and in the early morning), the disorder's underlying process may be different in infants than in older children and adults. The use of the label "asthma" to describe such children has important clinical consequences. It implies a syndrome in which there is airway inflammation and for which there is a specific protocol of management.

The younger the child, the greater the likelihood that an alternative diagnosis may explain recurrent wheeze. Alternative causes of recurrent wheezing in infancy include cystic fibrosis, recurrent milk inhalation, primary ciliary dyskinesia syndrome, primary immune deficiency, congenital heart disease, congenital malformation causing narrowing of the intrathoracic airways, and foreign body aspiration. Features such as a neonatal onset of symptoms, associated failure to thrive, vomiting-associated symptoms, and focal lung or cardiovascular signs all suggest an alternative diagnosis and indicate the need for further investigations, such as a sweat test to exclude cystic fibrosis, measurements of immune function, and reflux studies. Chest radiography is an important diagnostic test to exclude such alternative causes of wheezing.

Among those children in whom an alternative diagnosis has been excluded, there is the possibility that recurrent wheezing does not have a uniform underlying pathogenesis. Nonetheless, there are two general patterns of wheezing in infancy. Some infants who have recurrent episodes of wheeze associated with acute viral respiratory infections, often with a first episode in association with respiratory syncytial virus bronchiolitis, come from nonatopic families and have no evidence of atopy themselves. These infants usually outgrow their symptoms in the preschool years and have no evidence of subsequent asthma, though they may have minor defects of lung function and airway hyperresponsiveness. This syndrome may have more to do with airway geometry than airway inflammation, and thus may differ mechanistically from the more established chronic inflammatory condition that underlies asthma in older children and adults.

Other infants with asthma have an atopic background often associated with eczema and develop symptoms later in infancy that persist through childhood and into adult life. In these children, characteristic features of airway inflammation can be found even in infancy. However, there are no practical, clinical tests that can be done to establish the presence of airway inflammation. Also, there are no clear markers to predict the prognosis for an individual child. However, in young children with frequent wheezing, a parental history of asthma along with the presence of other atopic manifestations in the child is significantly associated with the presence of asthma at age 6. The onset of wheeze at an early age (under 2 years) is a poor predictor of whether asthma will persist in later childhood.

It is likely that the relationship between wheezing associated with recurrent viral infections and the later development of persistent asthma requires further study. Not only are the etiological mechanisms of asthma in childhood unclear, but there is also considerable reluctance on the part of doctors to establish a diagnosis and, therefore, to initiate appropriate therapy. Because lower respiratory tract symptoms similar to symptoms of asthma are so common in childhood (and frequently occur in association with upper respiratory tract symptoms), often

either a correct diagnosis is not made or an inappropriate diagnosis is given, thereby depriving the child of anti-asthma medication. Although in these young children there is the possibility of overtreatment, the episodes of wheezing may be foreshortened and reduced in intensity by the effective use of anti-inflammatory medications and bronchodilators rather than antibiotics. It is for this reason that health care professionals are encouraged to use the word "asthma" rather than other terminology to describe recurrent viral-associated wheezing in early childhood.

Asthma in all age groups may present only as repeated coughing, especially at night, with exercise, and with viral illness, but these are particularly common patterns of presentation of the disease in childhood. The presence of recurrent nocturnal cough in an otherwise healthy child should raise asthma as a probable diagnosis.

In children under the age of 5, the diagnosis of asthma has to be based largely on clinical judgment and an assessment of symptoms and physical findings. Because the measurement of airflow limitation and airway hyperresponsiveness in infants and small children requires complex equipment and is difficult, these measurements can only be recommended as a research tool. A trial of treatment is probably the most confident way to make a diagnosis of asthma in children (and in many adults as well). Prognostic features include a family history of asthma or eczema and the presence of eczema in a young child with respiratory symptoms. Children 4 to 5 years old can be taught to use a PEF meter and obtain reliable readings. However, unless there is careful parental supervision of when and how the measurements are made, PEF recording in childhood can be unreliable. The use of diary cards to record symptoms, PEF, and treatment has proved an invaluable part of asthma management strategies.

Some children with asthma present only with exercise-induced symptoms. In this group, or when there is doubt over the presence of mild asthma in a child, exercise testing is helpful. A 6-minute running protocol is easily performed in clinical practice. When used in conjunction with measurements of airflow limitation (FEV_1 or PEF), this can be most helpful in establishing a firm diagnosis of asthma, especially if the cough produced by the exercise is similar to that occurring spontaneously at night.

Asthma in the Elderly

A group of patients in whom the diagnosis of asthma is often not made or is missed is the elderly. Although lung damage from smoking or extensive exposure to inhaled environmental insults results in such diseases as bronchitis, emphysema, or fibrosing lung disease in this age group, it is now becoming increasingly recognized that undiagnosed asthma is a frequent cause of treatable respiratory symptoms. A further complicating factor is the difficulty that some older people have in performing lung function tests, including PEF. This means that making a diagnosis of asthma or chronic bronchitis based purely on symptoms is fraught with difficulties.

Late-onset asthma occasionally occurs in association with vasculitis and marked eosinophilia (Churg-Strauss syndrome). In the older patient, longstanding asthma may enter a severe destructive phase associated with allergic bronchopulmonary

aspergillosis. Characteristically, however, late-onset asthma is not associated with evidence for specific allergen sensitization.

Later in life, smoking and elevated serum IgE levels appear to be independent determinants of chronic airflow limitation, although they may interact. This has led to a growing body of opinion that chronic obstructive pulmonary disease (COPD), associated with a long history of smoking, may have an important inflammatory component that is responsive to anti-inflammatory drug intervention, thus blurring the boundary between asthma and other forms of obstructive lung disease. When doubt exists, a trial of oral glucocorticosteroids in which a greater than 12 percent improvement in FEV_1 or 15 percent improvement in PEF occurs, accompanied by improvement in symptoms and reduced bronchodilator requirement, usually confirms asthma as a cause of chronic respiratory symptoms.

The elderly are susceptible to episodes of wheezing, breathlessness, and cough caused by left ventricular failure (sometimes mistakenly labeled cardiac asthma). The presence of increased symptoms with exercise and at night may add to the diagnostic confusion. A careful history and physical examination looking for features of ischemic heart disease and cardiac dysfunction, together with an ECG and chest x-ray usually clarify the picture, but if after this doubt still persists, a trial of diuretic treatment is helpful.

Not only is the diagnosis of asthma difficult in the elderly, but the assessment of severity also presents a particular problem because the perception of symptoms and their severity is reduced in this age group when compared to young adults and also as a consequence of lifestyle adaptation.

Occupational Asthma

Asthma acquired in the workplace is a diagnosis that is frequently missed unless the health care professional is made aware of the possibility. Many inhalant chemicals are now known to produce asthma in the occupational environment (see Figure 3-4 titled "Agents Causing Asthma in Selected Occupations" in the original guideline document). They range from highly reactive small molecular weight chemicals such as isocyanates, to known immunogens such as platinum salts, as well as to complex plant and animal biological products. Because of its insidious onset, occupational asthma is often misdiagnosed as chronic bronchitis or some form of COPD and is therefore either not treated at all or treated inappropriately. The diagnosis requires a defined occupational history, especially in relation to exposure to sensitizing agents; absence of asthma symptoms before beginning employment; and a documented relationship between development of symptoms at the workplace and reduction of these on withdrawal from the workplace. A confirmation of occupational asthma may be successfully achieved by lung function measurement, such as serial measurement of PEF at work and away from work (single measurements are less sensitive than serial measurements), and specific bronchial provocation testing. The increasing recognition that occupational asthma can persist, or continue to deteriorate, even in the absence of continued exposure to the offending agent, emphasizes the need for an early diagnosis, appropriate strict avoidance of further exposure, and pharmacologic intervention.

Seasonal Asthma

In some sensitized individuals, asthma may be exacerbated by seasonal increases in specific aeroallergens. Examples include birch, grass, Alternaria, and ragweed pollens. Seasonal asthma is usually associated with allergic rhinitis. This type of asthma may occur only intermittently, with the patient being entirely asymptomatic between seasons. Alternatively, it may occur as a seasonal worsening of asthma symptoms in a patient with persistent asthma.

Cough Variant Asthma

Another group of patients whose asthma can sometimes be missed are those with cough variant asthma. These patients have chronic cough as their principal, if not only, symptom. Frequently this occurs at night; consequently evaluations during the day can be normal. For these patients, documentation of variability in lung function or of airway hyperresponsiveness, and possibly a search for sputum eosinophils, are particularly important. Within this group are patients who cough and have sputum eosinophils but who also have normal indices of lung function when assessed by spirometry and airway hyperresponsiveness.

Some patients with hypertension treated by angiotensin-converting-enzyme (ACE) inhibitors, or patients with gastroesophageal reflux, postnasal drip, or chronic sinusitis, may develop a cough that resembles cough variant asthma.

Differential Diagnosis

Asthma is one of the most common causes of respiratory symptoms, but it is only one cause of lung disease (see Figure 5-4 titled "Overview of Lung Diseases" in the original guideline document). An important step in ensuring diagnosis of asthma is the demonstration of reversible and variable airflow limitation, preferably by spirometry.

Although in children both asthma and acute respiratory infections produce wheezing as a consequence of widespread airway obstruction, respiratory symptoms may also arise from localized airway obstruction and inhaled foreign bodies, possibilities that must always be considered in the differential diagnosis (see Figure 5-5 titled "Differential Diagnosis of Obstructive Airway Disease" in the original guideline document). Another diagnosis to consider in both children and adults is pseudo-asthma, most often caused by vocal cord dysfunction. In adults, asthma superimposed on COPD is a common problem in past or present smokers.

Classification of Asthma

Asthma may be classified on the basis of etiology, severity, and pattern of airflow limitation.

Etiology

Many attempts have been made to classify asthma according to etiology, particularly with regard to environmental sensitizing agents. Such a classification is, however, limited by the existence of patients in whom no environmental cause

can be identified. Despite this, an effort to identify a specific environmental cause for asthma in an individual patient should be part of the initial clinical assessment, because it enables the use of avoidance strategies in asthma management.

Severity

Conventional assessments of asthma severity have combined assessments of symptoms, amounts of beta2-agonist used to treat symptoms, and lung function (see Figure 5-6, below). An assessment of asthma based on clinical or symptom indices of disease severity over the preceding year has been shown to relate to pathological indices of airway inflammation. Both the level of airflow limitation and its variability enable asthma to be subdivided by severity into four steps: Intermittent, Mild Persistent, Moderate Persistent, and Severe Persistent. This type of asthma classification, based on severity, is important when decisions must be made about management at the initial assessment of a patient. This is because asthma therapy involves a stepwise approach in which the level of therapy is increased as the severity of the asthma increases.

The severity of a patient's asthma may be classified into one of these four steps based on the clinical features present before treatment is begun (see Figure 5-6, below). When the patient is already on treatment, the classification of severity should be based on the clinical features present and the step of the daily medication regimen that the patient is currently on (see Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document). Thus, a patient with ongoing symptoms of mild persistent asthma, despite being on the appropriate maintenance treatment for this step, should be regarded as having moderate persistent asthma. Similarly, a patient with ongoing symptoms of moderate persistent asthma, despite being on the appropriate maintenance treatment for this step, should be regarded as having severe persistent asthma. Thus, the combination of the current level of symptoms and the current maintenance treatment step should enable the establishment of the patient's asthma severity and the corresponding appropriate maintenance treatment. Once asthma control is achieved and maintained for a sufficient time, then a reduction in therapy should be tested. If control is maintained, then the patient should be reclassified according to the new maintenance treatment. The severity of acute asthma exacerbations is often underestimated by patients, their relatives, and their health care professional. The reasons for this are complex, but include a failure to use measurements of lung function for assessment. If severe asthma exacerbations are not recognized and treated appropriately, such exacerbations can be fatal. It is important to recognize that any patient with asthma, however mild on a chronic basis, may have a severe acute asthma exacerbation. Specific factors have been identified that are associated with a higher risk of asthma mortality. These include a previous history of life-threatening acute attacks, hospitalization within the previous year, psychosocial problems, a history of intubation for asthma, recent reductions or cessation of glucocorticosteroid therapy, and noncompliance with recommended medical therapy.

Time Trends of Airflow Limitation

Asthma may also be classified according to time trend patterns of airflow limitation monitored by PEF measurements. This form of classification is likely to

reflect the different pathological causes of airflow limitation and has therapeutic implications. Intermittent asthma may be defined as the presence of occasional episodes of respiratory symptoms and PEF reductions (in the last year) with normal PEF and normal or near-normal airway responsiveness in between episodes. By contrast, persistent asthma is characterized by daytime and nocturnal PEF variability, frequent symptoms, and airway hyperresponsiveness. Some patients with longstanding persistent asthma with an irreversible component to their disease fail to achieve normal lung function despite intensive therapy with glucocorticosteroids. The term "brittle asthma" is sometimes used to describe patients with airway hyperresponsiveness and extreme day-to-day variability in airway obstruction. These patients are particularly at risk for sudden, severe, and life-threatening exacerbations.

Figure 5-6. Classification of Asthma Severity by Clinical Features Before Treatment

STEP 1: Intermittent

Symptoms less than once a week
Brief exacerbations
Nocturnal symptoms not more than twice a month

- FEV_1 or PEF $\geq$80% predicted
- PEF or FEV_1 variability <20%

STEP 2: Mild Persistent

Symptoms more than once a week but less than once a day
Exacerbations may affect activity and sleep
Nocturnal symptoms more than twice a month

- FEV_1 or PEF $\geq$80% predicted
- PEF or FEV_1 variability 20 to 30%

STEP 3: Moderate Persistent

Symptoms daily
Exacerbations may affect activity and sleep
Nocturnal symptoms more than once a week
Daily use of inhaled short-acting beta2-agonist

- FEV_1 or PEF 60 to 80% predicted
- PEF or FEV_1 variability >30%

STEP 4: Severe Persistent

Symptoms daily
Frequent exacerbations

Frequent nocturnal asthma symptoms
Limitation of physical activities

- FEV_1 or PEF $\leq$60% predicted
- PEF or FEV_1 variability >30%

A Six-Part Asthma Management Program

Asthma management has six interrelated parts:

1. Educate patients to develop a partnership in asthma management
2. Assess and monitor asthma severity with both symptom reports and, as much as possible, measurements of lung function
3. Avoid or control asthma triggers
4. Establish individual medication plans for long-term management in children and adults
5. Establish individual plans for managing exacerbations
6. Provide regular follow-up care.

Part 1: Educate Patients to Develop a Partnership in Asthma Management

Key Points

- Good asthma care requires sufficient numbers of well-educated health professionals organized so that they are available to the maximum number of patients. Guidelines on asthma management should be available but adapted and adopted for local use by local asthma planning teams consisting of both primary and secondary care health professionals (Evidence D).
- Implementation of guidelines is most likely to be effective and result in alteration of health professional behavior where there is practice-based education regarding the asthma guidelines, within-consultation prompting of behavior, and feedback to health care professionals regarding their management (Evidence B).
- Patient education involves a partnership between the patient and health care professional(s) with frequent revision and reinforcement. The aim is guided self-management, that is, giving patients the ability to control their own condition with guidance from the health care professionals. Interventions including the use of written self-management (action) plans have been shown to reduce morbidity in both adults (Evidence A) and children (Evidence B).
- Clear communication between health care professionals and asthma patients to meet patients' information needs is a key to enhancing compliance (Evidence B).

Education is clearly an essential part of the overall management of asthma. An outline summary of the relevance of education to asthma is shown in Figure 6-1 (below). Education includes education about primary prevention, secondary prevention, and management of asthma.

Figure 6-1. Education: An Essential Part of the Management of Asthma

Why educate?

Good education should reduce morbidity and mortality, keep people at work and school, and reduce health costs (especially if it reduces hospitalization) and indirect costs.

Who needs education?

- Policy makers and planners, so they make asthma a priority and effect good organization of care
- Health care professionals: doctors, nurses, pharmacists, medical students, and care assistants/field workers
- The wider public: teachers, employers, and coaches
- Patients (and their families and loved ones).

What topics should be covered in education?

- Information about the content of clinical practice guidelines
- Information about the diagnosis
- Information about prevention of exacerbations and deterioration of lung function
- Training in (guided) self-management
- Ability to recognize deteriorating asthma
- Knowledge about the different treatments
- Training in proper use of medication inhalers and peak flow meters.

How to educate?

- Educate the health care professionals and emphasize the importance of preventive management (i.e., managing asthma to prevent symptoms and exacerbations).
- Recognize that patient education involves:
    - giving information and acquisition of skills
    - altering behavior by the patient
- Good communication and development of a partnership between patients and health care professionals are essential if barriers to education are to be overcome.
- Monitoring, auditing, and setting of standards are also essential parts of the process and the responsibility of officials and professional organizations.

Where to educate?

- Education of health care professionals is necessary in schools and colleges, and by continuing medical education.
- Education of the wider public is necessary by articles in newspapers and journals and by programs on television.
- Education of patients is a continual process involving revision and

reinforcement at each meeting with a health care professional.

Patient Education

The aim of patient education, which is a continual process, is to provide the patient with asthma and the patient's family with suitable information and training so that the patient can keep well and adjust treatment according to a medication plan developed in advance with the health care professional. The emphasis must be on the development of an ongoing partnership among health care professionals, the patient, and the patient's family.

Patient education should aim to:

- Increase understanding
- Increase skills
- Increase satisfaction
- Increase confidence, and thereby to
- Increase compliance and self-management.

Basic education should be provided over several consultations or visits. Education should be provided to patients of all ages. Although the focus of education for small children will be on the parents, children as young as 3 years of age can be taught simple asthma management skills. Teenagers may have some unique difficulties regarding compliance that may be helped through peer support group education in addition to education provided by the health care professional. Revision and reinforcement are essential components of education provided by the health care professional. Figure 6-5, below, outlines the basic features of a patient education program and Figure 6-6 titled "Prevention: A Patient Checklist" in the original guideline document provides a patient checklist of what to avoid to prevent asthma exacerbation. The information and skill training required by individual patients vary, and each patient's ability or willingness to take responsibility similarly differs. Thus all individuals require certain core information and skills, but most education must be personalized and given to the patient in a number of steps. Social and psychological support may also be required to maintain positive behavioral change. Further, the patient's understanding of the information and management skills should be assessed periodically so that educational steps may be repeated or added as appropriate.

Figure 6-5. Individualizing Education in a Stepwise Manner

The goal: To provide the patient and his or her family with suitable information and training so that the patient can keep well and adjust treatment according to a medication plan developed with the health care professional.

Key components:

- The development of a partnership
- Acceptance that this is a continuing process
- A sharing of information
- Full discussion of expectations

- Expression of fears and concerns

The patient then requires information about:

- Diagnosis
- Difference between "relievers" and "controllers"
- Training in use of inhaler devices
- Advice regarding prevention
- Signs that suggest asthma is worsening and actions to take
- Training in monitoring asthma
- Advice about how and when to seek medical attention

The patient then requires:

- A guided self-management plan
- Regular supervision, revision, reward, and reinforcement

Improving Compliance

Studies of adults and children have shown noncompliance rates of around 50 percent with the taking of regular preventive therapies. Noncompliance may be defined in a nonjudgmental way as the failure of treatment to be taken as agreed upon by the patient and the health care professional. Noncompliance may be identified by prescription monitoring, pill counting, or drug assay, but at a clinical level it is best detected by asking about therapy in a way that acknowledges the likelihood of incomplete compliance (e.g., "So that we may plan therapy, do you mind telling me how often you find that you actually take the medicine?"). Specific drug and nondrug factors involved in noncompliance are listed in Figure 6-7 titled "Factors Involved in Noncompliance" in the original guideline document.

Compliance can usually be increased:

- If the patient accepts the diagnosis of asthma
- If the patient believes that his or her asthma may be dangerous or is a problem
- If the patient believes that he or she is at risk
- If the patient believes that the treatment is safe
- If the patient feels in control
- If there is good communication between patient and health care professional.

The importance of good communication as the basis for subsequent good compliance cannot be underestimated (Evidence B). Key factors in good communication are:

- A congenial demeanor (friendliness, humor, and attentiveness)
- Engaging in interactive dialogue
- Giving encouragement and praise
- Empathy, reassurance, and prompt handling of any concerns

- Giving of appropriate (personalized) information
- Eliciting shared goals
- Feedback and review

Methods of Delivery

Patients can acquire information about asthma and its treatment by:

- Listening to the health care professional
- Reading a book or cartoon, watching a video, or listening to an audiotape
- Attending an asthma educational course
- Attending a public meeting or a patient support group to learn from other patients with asthma
- Reading articles in magazines or newspapers
- Watching television programs or listening to the radio
- Using the World Wide Web or interactive multimedia.

Discerning which component of an intervention (giving information, closer medical care, self-management, or follow-up and enhanced supervision) has been most effective is not always easy. What is probably most effective is to give information verbally and then by several other routes, with those routes selected on the basis of patient education status and literacy level. Instruction via videos may be more appropriate than leaflets in some instances and has been shown to be useful in teaching good inhaler techniques. (Information about different types of inhalers and their use can be found on the Global Initiative for Asthma [GINA] Web site).

Many patients appear to benefit by being put in touch with patient support groups as a supplement to education by the health care professional. The format of these groups varies from country to country and from area to area, but most provide information materials, and many provide opportunities for group education, mutual support, and exchange of personal tips on managing asthma and coping with the stress a chronic disorder can present to patients and their families. Such patient support groups exist in a number of countries, and some are listed on the Global Initiative for Asthma (GINA) Web site.

Education at Initial Consultation

In early consultation the patient with asthma needs information about the diagnosis and simple information about the types of treatment available and about the rationale for the specific therapeutic interventions being recommended. For example, different inhaler devices should be demonstrated, and patients should take part in a decision as to which is most suitable for them. Some of these devices and techniques for their use are illustrated on the Global Initiative for Asthma (GINA) Web site. Additional devices are becoming available each year. It may be useful to use a criterion-based performance checklist for teaching patients about inhaler techniques. Patients should be advised about secondary prevention measures--for example, to avoid cigarette smoke as well as to avoid allergens, occupational sensitizing agents, and drugs known to cause asthma exacerbations in an individual. The consequences of ongoing exposure to such chronic pollutants and allergens even when the exposure does not always lead to an exacerbation should be explained. Advising patients to avoid such day-to-day triggers as exercise and cold air generally imposes inappropriate restrictions, and it is often

preferable to adjust treatment to prevent exacerbations precipitated by exposure to these.

Patients should be given adequate opportunity to express their expectations of both the asthma and its treatment. A frank appraisal should be made of how far their expectations may or may not be met, and agreement should be made about specific goals for therapy. In many cases, it is up to the health care professional to raise patients' level of expectations. It is reasonable for most patients to expect:

- Freedom from symptoms day and night
- No restriction on activities, including sports
- Best possible lung function (e.g., PEF)

At the initial consultation, verbal information should be supplemented by the provision of written (or pictorial, for low-literacy-level patients) information about asthma and its treatment. The patient and the patient's family should be encouraged to make note of any questions that arise from reading this information or as a result of the consultation. Patients should understand that time will be set aside for further information and for answering questions during each subsequent consultation.

During this initial visit, or a follow up consultation if necessary, the concept of PEF monitoring should be considered as appropriate to the patient's age, ability, and clinical assessment. Patients, especially those with more than mild disease, should receive training in how to measure and record PEF. The technique of rapid exhalation required for peak flow meter use is very different from the slow breathing required for using metered-dose inhalers (MDIs); this may be confusing to patients and thus requires careful instruction. When patients are taught how to record and interpret their PEF, it is helpful to explain that in addition to the absolute value of PEF, its variability is important. The patient should understand that such monitoring is undertaken to check on the effectiveness of therapy and to give early warning of potential deterioration. It may be helpful to stress that PEF monitoring is not done merely for the health care professional's record, but rather it provides critical information for making decisions about treatment, and thus PEF monitoring is a tool for patients to help themselves.

The aim then is for patients to be offered training in self-management techniques. A recent systematic review by the Cochrane Airways group of 22 studies involving patient education compared with usual care showed significant benefits in the intervention groups in terms of reduced morbidity and reduced use of health services. The effects were greatest where the intervention involved the issuing of written self-management action plans (Evidence A).

Guided Self-Management and Personal Asthma Action Plans

In guided self-management or asthma self-management, individual asthma patients make changes to their treatment in response to changes in the severity of their asthma, in accordance with predetermined guidelines. The process involves the integration of assessment and treatment, and incorporates written guidelines for both long-term treatment of asthma and treatment of

exacerbations. Follow-up and supervision by the health care provider is also an important contributor to the success of this strategy.

The concept of guided self-management arose as clinicians realized that delays in recognizing asthma exacerbations and initiating appropriate therapy are important factors contributing to asthma morbidity and mortality. Moreover, they knew that the majority of asthma attacks occur in the community and are managed by patients without immediate consultation with a doctor. This situation caused physicians to try to develop ways to teach asthma patients how to recognize and treat asthma attacks in accordance with current medical knowledge.

Guided self-management has been promoted in nearly all national and international asthma guidelines. The basic principles of guided self-management are shown in Figure 6-8 titled "The Basic Principles of Guided Self-Management in Adult Asthma" in the original guideline document.

Assessment

Fundamental to the success of guided self-management is the ability of the patient to recognize deterioration in asthma control. The patient must be taught to assess asthma severity by interpreting key symptoms and performing measurements of peak flow. Simple advice to seek medical attention if there are any nighttime symptoms, especially nocturnal wakening, or if symptoms do not respond to increased use of inhaled beta2-agonist therapy may be the most important message to convey. Domiciliary measurements of peak flow, with values interpreted as a percentage of normal predicted or previous best achieved recordings, are used as an objective assessment of the degree of airflow obstruction. Objective measurements are important because studies suggest that many patients are unable to reliably detect changes in their lung function, that is, they cannot correlate their subjective perception of asthma with measurements of lung function such as PEF. This diminished perception of lung function changes may correlate with the severity of the underlying asthma and is associated with an increased risk of death, so peak flow monitoring is particularly important in adults with severe asthma.

Follow-Up and Supervision

There is increasing evidence that self-management and inhaler skills need regular reinforcement by the health care professional. Moreover, a reduction in asthma therapy can only be adopted if the patient is seen regularly for follow-up.

At the follow-up consultation, the patient's questions are discussed, and any problems with asthma and its initial treatment are reviewed. Follow-up consultations at regular intervals should include checking the patient's inhaler technique and adherence to the medication plan and environmental control recommendations. Symptoms (and where appropriate, home peak flow recordings) noted in the patient diary are also reviewed regularly. Review of home PEF and symptom monitoring is necessary to assure that the goals of therapy are met and appropriate adjustments in therapy are made. After a period of initial training, the frequency of home peak flow and symptom monitoring depends in part on the severity of the patient's asthma. Patients with mild to moderate asthma with infrequent attacks can be advised to monitor their control during

exacerbations only, whereas patients with more severe or "brittle" asthma should undertake more regular monitoring.

Self-Management in Children

Just like adults, children with asthma (and their parents) need to know how to self-manage their own condition. Simple educational interventions (designed to teach self-management skills) among children admitted to the hospital with asthma have been shown to significantly reduce the readmission rate and reduce morbidity although conclusions about the relative effectiveness of the various components are limited by the lack of data on direct comparisons. This is especially important because asthma is a common reason for children to be admitted to the hospital, and this can cause considerable disruption to other family members and interfere with education.

Special Situations

Individualization of asthma therapy and the use of written guided self-management plans enable patients to cope with most situations, but trips away from home may require special planning. Particularly helpful may be a preholiday or pretravel check with the health care professional during which patients can get advice about taking along a sufficient quantity of routine and emergency medication, keeping the medication available during travel, remembering to take medication despite the different routine of a holiday, and checking in advance on how to find local medical attention if it should become necessary.

Pregnant patients may be counseled about possibilities for preventing the development of asthma in their babies. Although more research is needed, evidence suggests that breast feeding and reducing an infant's exposure to indoor allergens, especially domestic mites, and reducing exposure to maternal smoking could prevent the onset of asthma. This may be particularly relevant for the children of patients with allergies because atopy occurs in families and is the single most important risk factor for the development of asthma.

The Education of Others

The education of the general public about asthma is helpful in that it enables members of the public to recognize asthma symptoms and encourages those with asthma to seek medical attention and follow their asthma management program. Greater awareness of the condition is also likely to reduce feelings of stigmatization and to help dispel misconceptions that may exist about the condition.

Specific advice about asthma and its management should be offered to school teachers and physical education instructors, and several organizations produce such materials for this purpose. It is also helpful for employers to have access to clear advice about asthma. Most occupations are as suitable for those with asthma as for those without, but there may be some circumstances where caution is needed.

Part 2: Assess and Monitor Asthma Severity With Measurements of Symptoms and Measurements of Lung Function

Key Points

- Asthma severity can be judged by measurements of symptoms, measurements of lung function, and medication requirements.
- Pulmonary function studies are essential for diagnosing and assessing the severity of asthma in patients over 5 years old. Measures of lung function should also be used to monitor the course of asthma and the patient's response to therapy.
- PEF monitoring is an important clinical tool in the office, emergency department, and hospital, and is useful in the home.

Asthma severity can be judged by measurements of symptoms, measurements of lung function, and medication requirements (see the section titled "Diagnosis and Classification" above).

Measurements of Symptoms

Structured questionnaires to be filled in by the patient or by the health care professional can be used to quantify or score patients' reports of their different asthma symptoms over a period of time. Many such questionnaires have been developed, but few have as yet been validated against other objective measurements of asthma severity. However, carefully administered serial questionnaires can be a sensitive method for detecting a deterioration of asthma. The specific questions about symptoms should depend on the objectives of the questionnaire and the cultural setting. Particularly important questions in monitoring the patient's asthma and the patient's response to therapy are how frequently the patient is using reliever medication, and how frequently the patient has experienced nighttime symptoms such as cough, wheezing, or breathlessness. Questions about how frequently the patient limits normal activities may also be helpful. A visual analog scale to measure dyspnea has been demonstrated to be a reasonable tool for measuring and monitoring asthma severity in individual patients when more objective tests are not available.

Measurements of Lung Function

Lung function (pulmonary function) studies are essential for diagnosing and assessing the severity of asthma in patients over 5 years old. The measurements provide an indirect assessment of airway hyperresponsiveness, which may correlate with the degree of airway inflammation.

Measurements of lung function should also be used to monitor the course of asthma and the patient's response to therapy. Poor perception of the severity of asthma symptoms on the part of the patient and health care professional may be a major factor causing delay in treatment and thus may contribute to increased morbidity and mortality from asthma exacerbations. Patients who have access to PEF information may use their medication less frequently and more appropriately. Measurement of lung function for monitoring asthma is analogous to measurement in other chronic diseases.

Spirometry is recommended in the initial assessment of most patients with suspected asthma and periodically in selected patients to confirm home PEF measurements made with a peak flow meter. Subsequent measurement of PEF may be sufficient in most cases as the minimum objective parameter to follow in assessing symptoms and making therapeutic recommendations, when such recommendations depend on the severity of airflow limitation. For individual cases with complex questions related to their pulmonary function, periodic assessment in a specialized pulmonary testing facility should be considered.

PEF monitoring is an important clinical tool in the office, emergency department, and hospital, and is useful in the home. It is valuable to assess severity, assess degree of diurnal variation in lung function, monitor response to therapy during an acute exacerbation, detect asymptomatic deterioration of lung function in the home and office and intervene before it becomes more serious, monitor response to chronic therapy, provide objective justification for therapy to the patient, and identify triggers, including occupational sensitizers. Regular measurement of PEF in the health care professional's office is recommended. Monitoring PEF during the assessment of acute exacerbations in the health care professional's office or emergency department is essential.

Daily or twice daily PEF home monitoring by the patient is indicated in the initial assessment of the severity of the asthma and the response to therapy. Regular PEF home monitoring for several months or years may be especially useful to patients over 5 years of age with persistent asthma but might not be necessary for many patients. When priorities have to be set because of a shortage of PEF meters, continued home monitoring beyond initial assessment is particularly recommended for patients who have been hospitalized and for patients who are poor perceivers of their airflow limitation (i.e., they have difficulty recognizing early symptoms and are thus at increased risk for life-threatening asthma exacerbations). These patients might be identified during the initial monitoring and assessment period and by observing their perception of the severity of an acute exacerbation.

Measurement of PEF

Most adults, as well as children as young as 5 years of age, usually can perform a PEF measurement. The effort required to produce the measurement is a full inspiration to total lung capacity followed by a short maximal exhalation in a standing position. Because PEF measurement is effort dependent, patients need to be coached initially to give their best effort. For both spirometry and PEF measurements, it is essential to use correct techniques and equipment.

Ideally, PEF measurements should be taken twice daily, immediately upon arising and 10 to 12 hours later, before and after using a bronchodilator if a bronchodilator is needed. If PEF measurements are taken only once daily, they should be done in the morning upon arising and consistently before using a bronchodilator, if a bronchodilator is needed. A few patients will not comply, or their asthma will become extremely stable, and they may prefer to perform PEF measurements intermittently. Although this method loses the benefit of detecting early deterioration in lung function, it still provides important information about variability. If PEF is being measured only 2 or 3 times a week, it is best to do both a morning and an evening reading on the same day and consistently either before

or after using a bronchodilator, if a bronchodilator is taken, so that any variation greater than 20 percent (which indicates worsening of asthma) can be detected.

Interpreting PEF measurements. Predicted values of PEF are corrected for height, sex, race, and age, and normal limits of diurnal (or circadian) variability are available in the literature. However, in many patients, PEF values are consistently higher or lower than the average predicted values. It is recommended that PEF objectives for therapy be based on each patient's personal best and daily variability rather than on a percent of normal predicted value, particularly for patients with chronically impaired lung function.

Establishing personal best values and minimum diurnal variability when the patient is under effective treatment is important. During a monitoring period of 2 to 3 weeks, the patient should record PEF measurements at least twice a day. On both occasions the patient should measure the PEF 3 times and note the highest number. If the patient takes a bronchodilator, then PEF should be measured before and after using the bronchodilator. The personal best is the highest PEF measurement achieved when the patient's asthma is under control. If the patient's highest value during the monitoring period is less than 80 percent of predicted value after taking a bronchodilator (if the patient takes a bronchodilator), or daily variability is more than 20 percent again after taking a bronchodilator, more aggressive therapy and continued daily monitoring are indicated. A course of oral steroids in the initial evaluation period may be needed to establish personal best and minimum PEF daily variability.

The variability of PEF provides a reasonable index of asthma stability and severity. One method of describing diurnal PEF variability is as the amplitude (the difference between the prebronchodilator morning value and the postbronchodilator value from the evening before) expressed as a percentage of the mean daily PEF value. Another method is the minimum morning prebronchodilator PEF over 1 week, expressed as a percent of the recent best (Min%Max) (see Figure 5-3 titled "A Simple Index of PEF Variation" in the original guideline document). This latter method has been suggested to be the best PEF index of airway lability because it requires only a once-daily reading, it correlates better than any other index with airway hyperresponsiveness, and the calculation is simple.

Using PEF measurements to manage asthma. To help patients manage their asthma at home, a system of PEF zones can be used. This system correlates PEF measurements and variability with appropriate levels of medication to control asthma. The specific zones are established as a function of the individual's personal best or predicted value, whichever is highest, and/or daily variability. The emphasis is not on an isolated reading but rather on the variability from the patient's personal best or from one reading to the next.

Supervising home PEF monitoring. Several elements appear to be essential for the successful integration of home PEF monitoring into the treatment plan. The following guidelines should be used:

- Educate the patient and family about the purpose and technique of home monitoring. Education should include:
    - How and when to use the peak flow meter

    - How to record PEF measurements in a diary
    - How to interpret the measurements
    - How to respond to change
    - What information to communicate to the health care professional (including emergency department health care professionals)
- Explain how the health care professional uses the home PEF data to choose and evaluate treatment.

Part 3: Avoid Exposure to Risk Factors

Key Points

- Although pharmacological intervention to treat established asthma is highly effective in controlling symptoms and improving quality of life, every attention should be given to measures to prevent this chronic, lifelong, and incurable disease.
- Asthma exacerbations may be caused by a variety of triggers including allergens, pollutants, foods, and drugs. Tertiary prevention aims to reduce the exposure to these triggers to improve the control of asthma and reduce medication needs.

Three levels of prevention have been described and, in relation to asthma, include the following:

Primary prevention is introduced before exposure to risk factors known to be associated with a disease. The goal is to prevent the onset of disease in susceptible (at-risk) individuals. This is not yet possible in asthma. Increasing evidence indicates that allergic sensitization is the most common precursor to the development of asthma. Since sensitization can occur antenatally, much of the focus of primary prevention will likely be on perinatal interventions.

Secondary prevention is employed after primary sensitization to allergen(s) has occurred, but before there is any evidence of disease. The aim is to prevent the establishment of chronic, persistent disease in people who are susceptible and who have early signs of the disease. This is currently being investigated in asthma. Secondary prevention of asthma is likely to focus very specifically on the first year or two of life.

Tertiary prevention involves avoidance of allergens and nonspecific triggers when asthma is established. The goal is to prevent exacerbations or illness that would otherwise occur with exposure to identified allergens or irritants. It is considered that tertiary prevention should be introduced when the first signs of asthma have occurred. However, increasing evidence would suggest that the histopathology of the disease is fully established by the time asthma symptoms occur.

A prerequisite for establishing any form of preventive strategy is to have reliable markers that predict the progression of a disease, but to date there are no such markers available for asthma. At all levels of prevention, many of the issues remain speculative and have yet to be put to the test in proper long-term controlled clinical studies, though many such studies are in progress.

Primary Prevention

Potential Measures to be Applied Prenatally

There are no measures applied prenatally that can be recommended at this time for primary prevention. See the original guideline document for more information.

Potential Measures To Be Applied Postnatally

The most promising opportunities for primary prevention to be applied postnatally will be immunomodulation using Th1 immunoadjuvants, DNA vaccines, antigen in association with IL-12 or IFN-gamma, or oral administration of relevant gut microorganisms. However, all of these strategies currently remain in the realm of hypothesis and require appropriate investigation. See the original guideline document for more information.

Environmental Tobacco Smoke

No discussion of the primary prevention of asthma would be complete without considering the impact of environmental tobacco smoke. The health effects of passive smoking have been extensively reviewed. The data related to parental smoking and lower respiratory illness in exposed children up to 3 years of age indicate a direct causal relationship between these factors. However, it is impossible to distinguish the independent contributions of prenatal and postnatal maternal smoking. In-depth studies of lung function immediately after birth have shown that maternal smoking during pregnancy has an influence on lung development. Further, infants of smoking mothers are 4 times more likely to develop wheezing illnesses in the first year of life. In contrast, there is little evidence (based on meta-analysis) that maternal smoking during pregnancy has an effect on allergic sensitization. Thus, smoking during pregnancy has an impact on lung development, which increases the frequency of nonallergic wheezing illnesses in infancy, but has less impact on later allergic asthma. Overall, these observations are sufficient to make the very firm conclusion that environmental tobacco smoke exposure both prenatally and postnatally has an adverse influence on wheezing illnesses (Evidence A).

Secondary Prevention

Once allergic sensitization has occurred, there are additional opportunities to prevent the actual development of asthma. Two studies have suggested that pharmacologic intervention with H1 antihistamines may reduce the onset of wheezing in young children who present initially with atopic dermatitis. However, these studies need confirmation before it can be proposed that this class of compounds can prevent the onset of asthma. An older study found that allergen-specific immunotherapy may reduce the onset of asthma. The Preventive Allergy Treatment (PAT) Study results indicate that immunotherapy reduces the development of asthma in children with seasonal rhinoconjunctivitis.

Observations of occupational allergy suggest that early cessation of exposure to an offending allergen, after there is evidence of sensitization and symptoms, is

more likely to lead to a total resolution of symptoms than if the exposure continues.

Tertiary Prevention

Asthma exacerbations may be caused by a variety of triggers including allergens, pollutants, foods, and drugs. Tertiary prevention aims to reduce the exposure to these triggers to improve the control of asthma and reduce medication needs.

Avoidance of Indoor Allergens

The occurrence and severity of asthma symptoms are related to environmental allergens. Thus, indoor environmental control measures to reduce exposure to allergens might be important, although it is difficult to achieve complete control, and there is conflicting evidence about whether such control measures are effective at reducing asthma symptoms. The majority of single interventions have failed to achieve a sufficient reduction in allergen load to lead to a clinical improvement. It is likely that no single intervention will achieve sufficient benefits to be cost effective. However, among inner city children with atopic asthma, an individualized, home-based, comprehensive environmental intervention was shown to reduce asthma morbidity.

The effectiveness of allergen reduction in the treatment of asthma was first suggested by studies in which patients were removed from their homes to a low-allergen environment at high altitude. However, the real challenge is to create a low-allergen environment in patients' homes. Effective control strategies should be tailored to individual allergens, flexible to suit individual needs, and cost effective.

Among the wide variety of allergens that occur within human dwellings are domestic mites, animal allergens (furred animals), cockroach allergen, and fungi.

Domestic mites. No single measure is likely to reduce exposure to mite antigen but an integrated approach including barrier methods, dust removal, and reduction of microhabitats favorable to mites is recommended (Evidence C) (see Figure 7-1).

Little is known about the influence of different types housing on mite populations. The introduction of blankets increases the number of mites in homes dramatically, and has been shown to be associated with the occurrence of asthma in adults, but not in children. Carpets are also an important microhabitat, and a possible source of reinfestation of bedding. High levels of humidity are essential for mite population growth, and reducing humidity has been shown to be effective control method in some but not all studies. Some investigations have shown that use of mattress, pillow and duvet covers that are impermeable to mite allergens are effective (Evidence B), but others have shown no effect of these measures in reducing symptoms in adults with asthma or allergic rhinitis. Other mite avoidance methods have been advocated (Figure 7-1), but for most their effect on symptoms has not been adequately tested. Due to the aerodynamic characteristics of mite allergens, air filtration units and ionizers are ineffective at reducing exposure.

Figure 7-1. Measures for Reducing Exposure to Domestic Dust Mite Allergens

- Encase mattress, pillow, and quilt in impermeable covers
- Wash all bedding in the hot cycle (55 to 60 degrees C) weekly
- Replace carpets with linoleum or wood flooring
- Treat carpets with acaricides and/or tannic acid
- Minimize upholstered furniture/replace with leather furniture
- Keep dust-accumulating objects in closed cupboards
- Use a vacuum cleaner with integral high efficiency particulate air (HEPA) filter and double-thickness bags
- Replace curtains with blinds or easily washable (hot cycle) curtains
- Hot wash/freeze soft toys.

Animal allergens. Furred, warm-blooded animals, including small rodents, produce dander, urine, and saliva that can cause allergic sensitization and subsequent reactions. Complete avoidance of pet allergens is impossible, as the allergens are ubiquitous and can be found in many environments outside the home, including schools, public transportation, and even cat-free buildings. Removal of such animals from the home is important, but even after permanent removal of the animal it can be many months before reservoir allergen levels decrease. In patients who are allergic to cats or dogs and persist in keeping their pet, exposure-reduction measures listed in Figure 7-2, below, may be considered. However, the clinical effectiveness of these measures remains unproven and there are many conflicting data on this subject.

Figure 7-2. Measures for Reducing Exposure to Animal Allergens

- Keep the pet out of the main living areas and bedrooms
- Install HEPA air cleaners in the main living areas and bedrooms
- Have the pet washed twice a week, although some studies report this to be ineffective
- Thoroughly clean upholstered furniture/replace with leather furniture
- Replace carpets with linoleum or wood flooring
- Use a vacuum cleaner with integral HEPA filter and double-thickness bags

Cockroach allergen. Cockroach infestation is an important cause of allergic sensitization, particularly in inner-city homes. Avoidance measures for cockroaches include eliminating suitable environments (restricting havens by caulking and sealing cracks in the plaster work and flooring, controlling dampness, and reducing the availability of food), restricting access (sealing entry sources such as around paperwork and doors), chemical control (abamectin), and traps. However, these measures are only partially effective.

Fungi. The number of fungal spores can best be reduced by removing or cleaning mold-laden objects. Maintaining a low humidity (less than 50 percent) is important. Air conditioners and dehumidifiers reduce humidity and filter large fungal spores, lowering the mold and yeast count indoors, although their benefit in terms of reducing asthma symptoms is controversial. In tropical and subtropical

climates, fungi may grow on the walls of the house due to water seepage and humidity. To avoid this, the walls could be tiled or cleaned as necessary.

Avoidance of Outdoor Allergens

Outdoor allergens such as pollens and molds are impossible to avoid completely. Exposure may be reduced by closing windows and doors, remaining indoors when pollen and mold counts are highest, and using air conditioning if possible. Some countries use radio, television, and the Internet to provide information on outdoor allergen levels. Knowledge of a patient's sensitivity to specific allergens may be useful for giving advice about the timing and location of the patient's travel.

Avoidance of Indoor Air Pollutants

The most important measure is to avoid passive and active smoking. Passive smoking increases the risk of allergic sensitization in children. It also increases the frequency and severity of symptoms in children with asthma. Parents of children with asthma should be advised not to smoke and not to allow smoking in rooms their children use. Active cigarette smoking reduces treatment efficacy of inhaled and systemic glucocorticosteroids (Evidence B) and smoking cessation needs to be vigorously encouraged.

The major indoor air pollutants are respirable particles, nitric oxide, nitrogen oxides, carbon monoxide, carbon dioxide, sulfur dioxide, formaldehyde, and biologicals such as endotoxin. Preventing and controlling indoor air quality problems--except by cigarette smoke avoidance--can be expensive and time consuming, and the effectiveness of most control methods has not been adequately evaluated. The principal steps known to reduce exposure to respirable particles are avoiding cigarette and other tobacco smoke, venting all furnaces to the outdoors, and maintaining heating systems adequately. To reduce exposure to nitric oxide, nitrogen oxides, and carbon monoxide, all gas appliances should have sufficient flues or ducts (Evidence B). Adequate ventilation will decrease carbon dioxide concentration. Avoiding wood smoke, household sprays, and volatile organic compounds (e.g., polishes and cooking oils) is also important (Evidence D).

Avoidance of Outdoor Air Pollutants

Several studies have implicated various pollutants as aggravating asthma, mainly in controlled chamber exposure experiments. Most epidemiological studies show a significant association between air pollutants--such as ozone, nitrogen oxides, acidic aerosols, and particulate matter--and symptoms or exacerbations of asthma. On occasion, weather and atmospheric conditions create a period of intense air pollution in a defined geographic area. Useful steps to consider for patients with asthma during such air pollution episodes include:

- Avoid unnecessary physical activity. Cold temperature and low humidity are additionally stressful to the patient with asthma who exercises under conditions of high air pollution.
- Avoid smoking and smoke-filled rooms.
- Avoid exposure to dust and other irritants such as hair spray, paint, exhaust fumes, or smoke from any fire.

- Avoid exposure to persons with respiratory infections.
- Try to stay indoors in a clean environment. Air conditioning and other filters may be helpful. When it is necessary to go outdoors, it is recommended to take a rapid-acting inhaled bronchodilator beforehand in order to prevent acute symptoms.
- If it appears that the air pollution episode will persist or worsen, it may be a good idea to leave the polluted area temporarily.
- The health care professional and patient should formulate special plans to be followed with regard to medication use.

Avoidance of Occupational Exposure

A large number of substances have been identified as occupational allergens and as risk factors that can cause asthma. Levels above which sensitization frequently occurs have been proposed for many chemicals. However, once a patient has been sensitized, the level of exposure necessary to induce symptoms may be extremely low, and resulting exacerbations may become increasingly severe. Attempts to reduce occupational exposure have been successful especially in industrial settings, and some potent sensitizers, such as soy castor bean, have been replaced by less allergenic or sensitizing substances. Prevention of latex allergy has been made possible by the production of hypoallergenic gloves, which are powder-free and have a lower allergen content. Although more expensive than untreated gloves, they are cost effective. The early identification of occupational sensitizers and the removal of sensitized patients from any further exposure are important aspects of the management of occupational asthma (Evidence B).

Food Avoidance

Food allergy as an exacerbating factor for asthma is uncommon and occurs primarily in young children. Food avoidance should preferably not be recommended before a double-blind food challenge has been made. When the outcome of such a challenge is positive, food allergen avoidance can reduce asthma exacerbations.

Sulfites (common food and drug preservatives found in such foods as processed potatoes, shrimp, dried fruits, beer, and wine) have often been implicated in causing severe asthma exacerbations and occasional deaths. They should be avoided by sensitive patients. Proof for the involvement of other dietary substances, including the yellow dye tartrazine, benzoate, and monosodium glutamate, is difficult to ascertain, and their role in exacerbating asthma is probably minimal. Confirmation of their relevance requires a double-blind challenge before making specific dietary restrictions.

Avoidance of Certain Drugs

Some medications can exacerbate asthma. Aspirin and other nonsteroidal anti-inflammatory agents can cause severe exacerbations and should be avoided in patients with a history of reacting to these agents. Beta-blocker drugs administered orally or by eye drops may exacerbate bronchospasm and in general, should not be used by patients with asthma. If they are used, close medical supervision is essential. Avoidance of these drugs prevents exacerbations in susceptible patients.

Vaccination

Patients with moderate to severe asthma might be advised to receive an influenza vaccination every year or at least when vaccination of the general population is advised. However, routine influenza vaccination of children and adults with asthma does not appear to protect them from asthma exacerbations. Inactivated influenza vaccines are associated with few side effects, and are safe to administer to asthmatic adults and children over the age of 3 years, including those with severe asthma. There are data to suggest that intra-nasal vaccination may be associated with an increased incidence of asthma exacerbations in children under age 3.

Part 4A. Establish Medication Plans for Long-Term Asthma Management in Adults

Key Points

- Preferred treatment recommendations in this report are based on efficacy and safety outcomes in populations. The response of individual patients may, of course, differ significantly from the mean response of the population. Decisions about treatment are often a compromise between what the physician recommends and what the patient is prepared to take.
- Medications for asthma can be administered in different ways, including inhaled, oral (ingested), and parenteral (subcutaneous, intramuscular, or intravenous). The major advantage of delivering drugs directly into the airways via inhalation is that high concentrations can be delivered more effectively to the airways, and systemic side effects are avoided or minimized.
- Although no cure for asthma has yet been found, it is reasonable to expect that in most patients with asthma, control of the disease can and should be achieved and maintained.
- Control of asthma can be achieved in many patients and can be defined as:
    - Minimal (ideally no) chronic symptoms, including nocturnal symptoms
    - Minimal (infrequent) exacerbations
    - No emergency visits
    - Minimal (ideally no) need for p.r.n. (as needed) beta2-agonist
    - No limitations on activities, including exercise
    - PEF circadian variation of less than 20 percent
    - (Near) normal PEF
    - Minimal (or no) adverse effects from medicine.
- Therapy should be selected on the basis of the severity of a patient's asthma, availability of anti-asthma medications, conditions of the health care system, and individual patient circumstances.
- For intermittent asthma, no daily medication is recommended for the vast majority of patients. Treatment of exacerbations should depend on the severity of the exacerbation. A rapid-acting inhaled beta2-agonist may be taken as needed to relieve asthma symptoms. The occasional patient with intermittent asthma, but severe exacerbations, should be treated as having moderate persistent asthma.
- Patients with mild persistent asthma require controller medication every day to achieve and maintain control of their asthma. Treatment with an inhaled glucocorticosteroid is preferred. Other options are a sustained-release theophylline, cromones, or a leukotriene modifier.

- The preferred therapy for moderate persistent asthma is regular treatment with a combination of inhaled glucocorticosteroid and a long-acting inhaled beta2-agonist twice daily. Sustained-release theophylline or a leukotriene modifier is an alternative to the beta2-agonist in this combination therapy. An alternative to combination therapy is a higher dose of inhaled glucocorticosteroid.
- The primary therapy for severe persistent asthma includes inhaled glucocorticosteroid at higher doses plus a long-acting inhaled beta2-agonist twice daily. Alternatives to the long-acting inhaled beta2-agonist for add-on treatment are an oral sustained-release theophylline, leukotriene modifier, or oral beta2-agonist. These drugs may also be added to the combination of high-dose inhaled glucocorticosteroid and long-acting inhaled beta2-agonist if necessary.
- Once control of asthma is achieved and maintained for at least 3 months, a gradual reduction of the maintenance therapy should be tried in order to identify the minimum therapy required to maintain control.

The Medications

Route of Administration

Medications for asthma can be administered via different ways, including inhaled, oral (ingested), and parenteral (subcutaneous, intramuscular, or intravenous). The major advantage of delivering drugs directly into the airways via inhalation is that high concentrations can be delivered more effectively to the airways, and systemic side effects are avoided or minimized. Some of the drugs that are effective in asthma can only be used via inhalation because they are not absorbed when given orally (e.g., anticholinergics and cromones). The onset of action of bronchodilators is substantially quicker when they are given via inhalation than when these drugs are administered orally.

Aerosolized medications that are used to treat asthma are available as pressurized metered-dose inhalers (MDIs), breath-actuated MDIs, dry powder inhalers (DPIs), and nebulized or "wet" aerosols. Patients should be instructed in the use of the inhaler device, and their technique should be checked regularly. Inhaled asthma medications can be given either singly or in combination inhalers, the latter of which most often contain a glucocorticosteroid and a bronchodilator.

The disadvantage of pressurized MDI therapy is that training and skill are required to coordinate activation of the inhaler and the inhalation. The use of a spacer (holding chamber) improves drug delivery from an MDI (Evidence A). The spacer device allows discharge of the drug into a chamber where particles of medications are held in suspension for 10 to 30 seconds. During this time, the patient can inhale the drug. Spacers also reduce deposition in the mouth and oropharynx, decreasing cough as well as the possibility of oral candidiasis when used to deliver glucocorticosteroids (Evidence A). Further, the use of spacers for the delivery of inhaled glucocorticosteroids decreases their systemic bioavailability and the risk of systemic side effects (Evidence B). Some studies suggest that high doses of rapid-acting inhaled beta2-agonists administered from MDIs using spacer devices achieve bronchodilatation equivalent to that effected by nebulization in treating severe exacerbations. A systematic review comparing MDI-plus-spacer versus wet-nebulizer delivery of high-dose rapid-acting inhaled beta2-agonists in patients

with severe acute exacerbations of asthma showed these two delivery systems lead to equivalent clinical outcomes in adults but the MDI-plus-spacer system yields better clinical outcomes in children (Evidence B). Breath-actuated aerosols may be helpful for patients who have difficulty using the pressurized MDI.

DPIs do not utilize freon propellants. They require an inhalation technique that is different from the MDI technique, and are generally easier to use. A minimal inspiratory flow rate is necessary to inhale from a DPI, and thus the DPI may be difficult for some patients to use during an exacerbation. The dosage should be adjusted to ensure adequate drug delivery at the inspiratory flow rate that patients can achieve. Some DPIs deliver pure drug, while others deliver the drug mixed with a filler (such as lactose), and thus the dosage should also take into account the fact that different DPIs yield different drug delivery to the lung. The dose of therapy may need to be adjusted when switching from an MDI to a DPI. DPIs are more ecological than MDIs because they do not utilize chlorofluorocarbons (CFCs), but storage of some dry powder formulations may be more difficult in humid climates.

The CFCs in MDIs are now being replaced by hydrofluoroalkanes (HFAs), and the medication insert for dosage of the HFA preparations should be carefully reviewed by the clinician. For bronchodilators the doses from CFC and HFA inhalers appear to be equivalent. However, for some glucocorticosteroids the HFA formulations, which deliver a greater fraction of smaller particles to the lung, may result in both greater efficacy and greater systemic effects.

Controller Medications

Controller medications, medications used daily on a long-term basis to achieve and maintain control of persistent asthma, include inhaled glucocorticosteroids, systemic glucocorticosteroids, sodium cromoglycate (cromolyn sodium), nedocromil sodium, sustained-release theophylline, long-acting inhaled beta2-agonists, long-acting oral beta2-agonists, leukotriene modifiers, and systemic steroid-sparing therapies. Inhaled glucocorticosteroids are at present the most effective controller medications.

See the original guideline document for details.

Reliever Medications

Reliever medications-medications that act quickly to relieve bronchoconstriction and its accompanying acute symptoms include rapid-acting inhaled beta2-agonists, systemic glucocorticosteroids, inhaled anticholinergics, short-acting theophylline, and short-acting oral beta2-agonists.

See the original guideline document for details.

Alternative and Complementary Methods of Healing

See the original guideline document for a detailed discussion of options.

A Stepwise Approach to Pharmacologic Therapy

Although no cure for asthma has yet been found, it is reasonable to expect that in most patients with asthma, control of the disease can and should be achieved and maintained. Control of asthma is defined as:

- Minimal (ideally no) chronic symptoms, including nocturnal symptoms
- Minimal (infrequent) exacerbations
- No emergency visits
- Minimal (ideally no) use of p.r.n. (as needed) beta2-agonist
- No limitations on activities, including exercise
- PEF circadian variation of less than 20 percent
- (Near) normal PEF
- Minimal (or no) adverse effects from medicine.

Choice of Therapy

The selection of pharmacologic treatment options is made on the basis of asthma severity, the patient's current treatment, the pharmacological properties and availability of antiasthma treatment, and economic considerations. Because asthma is a dynamic as well as chronic condition, medication plans need to accommodate variability among patients as well as within individual patients over time. An essential aspect of any treatment plan is the need for monitoring the effect of the treatment (including use of measurements of lung function and symptoms) and adapting the treatment to the variability of the asthma.

An approach to pharmacologic therapy that correlates with asthma severity permits this flexibility. As discussed previously, the classification of asthma severity should include symptom and medical history evaluation, current treatment, clinical examination, and measurements of lung function where possible.

An appropriate approach to therapy recommends that the number (type), dose, and eventually the frequency of medications are increased with increasing asthma severity. The aim is to accomplish the goals of therapy with the least possible medication. Thus in developing an asthma management plan, the health care professional must judge whether to give maximum treatment at the onset, which may include a burst or cycle of oral glucocorticosteroids and/or full doses of inhaled glucocorticosteroids plus long-acting beta2-agonists (Evidence D) in order to achieve control of the patient's asthma as quickly as possible, and then decrease the medication, or to start with treatment judged appropriate for the severity of the patient's asthma and increase treatment gradually if necessary. Once control is sustained for about 3 months, a reduction in therapy to a lower step can be carefully considered. This reduction in therapy is needed to identify the minimum therapy required to maintain control.

Few studies have as yet investigated the efficacy of various comprehensive therapeutic programs in accomplishing a broad set of therapeutic goals for controlling asthma. The recommendations that follow are thus based on an understanding of the pathology of asthma and an extrapolation from controlled clinical therapeutic trials that have evaluated the effects of particular antiasthma therapies on separate outcomes such as asthma symptoms, lung function, and the use of bronchodilators on an as-needed basis to relieve symptoms.

Figure 7-5, below, presents the stepwise approach to therapy to achieve and maintain control of asthma in adults. The step system for classifying asthma severity takes into account the treatment that the patient is currently receiving (see Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document). Figure 7-5 presents all therapies that can be recommended for treating each step of asthma severity. Guidance for selecting among these available modalities is provided in the text of the original guideline document. The cost of the medication is an obvious factor in determining choice of treatment. Cost of treatment varies from country to country and is only one of the factors that contribute to the total cost of a disorder such as asthma.

Figure 7.5. Recommended Medications by Level of Severity: Adults and Children Older Than 5 Years of Age

All Levels: In addition to regular daily controller therapy, rapid-acting inhaled beta2-agonist* should be taken as needed to relieve symptoms, but should not be taken more than 3 to 4 times a day. Patient education is essential at every level.		
Level of Severity:**	Daily Controller Medications:	Other Treatment Options:***
Step 1. Intermittent asthma****	None necessary	
Step 2. Mild Persistent Asthma	Low-dose inhaled glucocorticosteroid (see original guideline document for dosage information)	• Sustained-release theophylline, OR • Cromone, OR • Leukotriene modifier
Step 3. Moderate Persistent Asthma	Low-to-medium inhaled glucocorticosteroid plus long-acting inhaled beta2-agonist	• Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS sustained-release theophylline, OR • Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS long-acting oral beta2-agonist, OR • High-dose inhaled glucocorticosteroid (see original guideline document for dosage information), OR • Medium-dose inhaled glucocorticosteroid (see original guideline

All Levels: In addition to regular daily controller therapy, rapid-acting inhaled beta2-agonist* should be taken as needed to relieve symptoms, but should not be taken more than 3 to 4 times a day. Patient education is essential at every level.		
Level of Severity:**	Daily Controller Medications:	Other Treatment Options:***
		document for dosage information) PLUS leukotriene modifier
Step 4. Severe Persistent Asthma	High-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS long-acting inhaled beta2-agonist, PLUS one or more of the following, if needed: • Sustained-release theophylline • Leukotriene modifier • Long-acting oral beta2-agonist • Oral glucocorticosteroid • Immunoglobulin E (IgE)*****	
All Levels: Once control of asthma is achieved and maintained for at least three months, a gradual reduction of the maintenance therapy should be tried in order to identify the minimum therapy required to maintain control.		

Other options for reliever medications are (in increasing order of cost) inhaled anticholinergic, short-acting oral beta2-agonist, and short-acting theophylline.
** See Figure 5-6, above, and Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document for information regarding classification of severity.
*** Other treatment options listed in order of increasing cost. Relative medication costs may vary from country to country.
**** Those with intermittent asthma but severe exacerbations should be treated as having moderate persistent asthma (Evidence D).
*****Current evidence supports use in adults and children aged 12 years and above only.

How to Achieve and Maintain Control of Asthma

This section of the original guideline document describes the therapy appropriate for different steps of asthma severity. The presence of one or more features of clinical severity places a patient at the respective step (see Figure 5-6, above). The current treatment should be included in the assessment of severity (see Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document).

In the stepwise approach to therapy, progression to the next step is indicated when control is not achieved or is lost with the current treatment, and there is assurance the patient is using medication correctly. The frequent (e.g., more than 3 times a week) presence of such symptoms as cough, wheezing, and dyspnea, and the increased use of rapid-acting bronchodilators may indicate inadequate control of asthma. The presence of symptoms at night or early in the morning is an especially useful indicator. Measurement of PEF and its variability is helpful in

the initial assessment of asthma severity and in monitoring the initial treatment, assessing changes in severity, and preparing for a reduction in therapy.

The treatments suggested for each step are guidelines only. See the original guideline document for details. Specific medication plans should be tailored by the health care professional depending on the availability of antiasthma medication, the conditions of the health care system, and individual patient circumstances. Repeated use of reliever medication more than 4 times a day indicates that the patient's asthma is not well controlled, and the intensity of treatment should be increased.

Seasonal Asthma

A patient has seasonal asthma when he or she has asthma symptoms due to seasonal exposure to allergen. This may be intermittent in patients who are otherwise entirely asymptomatic with normal PEF values between seasons, or it may occur as a seasonal worsening of persistent asthma. The severity varies from patient to patient and from season to season. Treatment will vary accordingly but should follow the recommendations for the treatment of persistent asthma. Ideally, treatment should start just before the expected season or upon the first symptoms, and can be stopped at the end of the season when symptoms or lung function abnormalities are no longer present (Evidence D).

Part 4B: Establish Medication Plans for Long-Term Asthma Management in Infants and Children

Key Points

- Childhood and adult asthma share the same underlying pathophysiological mechanisms. However, because of the processes of physical and cognitive growth and development, the effects, and adverse effects, of asthma and asthma treatments in children differ from those in adults.
- Many asthma medications (e.g., glucocorticosteroids, beta2-agonists, theophylline) are metabolized faster in children than in adults, and young children tend to metabolize drugs faster than older children.
- Therapy should be selected on the basis of the severity of asthma in the individual patient, the availability of anti-asthma medications, the characteristics of the health care system, and the individual patient's social, family, and economic circumstances.
- Inhaled glucocorticosteroids are at present the most effective controller medications and are therefore recommended for persistent asthma at any step of severity. Long-term treatment with inhaled glucocorticosteroids markedly reduces the frequency and severity of exacerbations.
- Long-term treatment with inhaled glucocorticosteroids has not been shown to be associated with any increase in osteoporosis or bone fracture. Studies including a total of over 3,500 children treated for mean periods of 1 to 13 years have found no sustained adverse effect of inhaled glucocorticosteroids on growth.
- Rapid-acting inhaled beta2-agonists are the most effective reliever therapy in asthma, and this class of drugs has been the mainstay of asthma treatment in children for many years. These drugs are the most effective bronchodilators

available and are therefore the treatment of choice for acute asthma symptoms.
- Once control of asthma is achieved and maintained for at least 3 months, a gradual reduction of the maintenance therapy should be tried in order to identify the minimum therapy required to maintain control.

In developing a treatment plan, factors such as the severity of the individual patient's asthma, the benefits, risks, and availability of each treatment, cultural preferences, and the characteristics of the health care system need to be considered. The final choice of treatment should integrate the individual clinician's expertise with the patient's preferences and the best available evidence from systematic, clinically relevant research in children.

The Medications

Medications for the management of pediatric asthma include both controllers and relievers. Controllers are medications taken daily on a long-term basis to achieve and maintain control of asthma. Relievers act quickly to relieve bronchoconstriction and its accompanying acute symptoms such as wheezing, chest tightness, and cough.

Many asthma medications (e.g., glucocorticosteroids, beta2-agonists, theophylline) are metabolized faster in children than in adults, and young children tend to metabolize drugs faster than older children. Although this rapid metabolism to inactive drug is advantageous from a safety perspective, it also means that when medication is administered orally, higher doses should be given to young children than to adults or older children.

Route of Administration

Medications for asthma can be administered via different ways, including inhaled, oral (ingested), and parenteral (subcutaneous, intramuscular, or intravenous). The major advantage of delivering drugs directly into the airways via inhalation is that high concentrations can be delivered more effectively to the airways, and systemic side effects are avoided or minimized. Some of the drugs that are effective in asthma can only be used via inhalation because they are not absorbed when given orally (e.g., anticholinergics and cromones). The onset of action of bronchodilators is substantially quicker when they are given via inhalation than when these drugs are administered orally. The choice of inhaler device should emphasize the efficacy of drug delivery, cost effectiveness, safety, and convenience.

Information about lung dose for a particular drug formulation is seldom available for children. Differences between devices do not alter the potential maximum effect of a given drug, but they do result in different potencies for the same nominal dose of the drug given by different inhalers. If these differences are disregarded, clinically important over-or under-treatment may be seen. Dose recommendations need to be evaluated depending on the device to be used.

The choice of device for maintenance treatment should be related to the class of drug. The actual dose of beta2-agonist administered by inhaler is often greater than necessary, but the potential side effects are minimal. Due to the greater

potential for side effects, however, inhaled glucocorticosteroids merit a more careful choice of device to ensure an optimal therapeutic effect with minimal side effects. The differences in first-pass metabolism of different inhaled glucocorticosteroids should also influence the choice of device. A spacer is advised when administering beclomethasone, flunisolide, triamcinolone, or budesonide by pressurized MDI. A spacer is not required for budesonide delivered from a turbuhaler.

For maximum convenience, an inhaler device should be freely portable with no power requirement, and technically simple to operate with minimal maintenance requirements. Simplicity of operation is especially important in the treatment of infants and preschool children, who are often cared for by different people at different times of day (and night). Cooperation and coordination required to use a device should be minimal. Passive cooperation, such as the acceptance of a face mask, can be expected from most preschool children and even infants. Active cooperation, such as performing specific inhalation maneuvers and priming or activating a device, can only be expected in older children.

For infants and preschool children, in whom active cooperation cannot be expected, a pressurized MDI used with a spacer and face mask is the device of choice for maintenance treatment. As cooperation improves, often around the age of 4 to 6 years, the child should be encouraged to use a mouthpiece rather than a face mask to inhale from the spacer. From the age of 6, a DPI or breath-activated MDI is the device of choice (see Figure 7-6 titled "Choice of Inhaler Device for Children" in the original guideline document). Even for administration of inhaled beta2-agonists during episodes of severe acute asthma, the nebulizer can be replaced by pressurized MDI with a spacer.

Nebulizers are not preferred for maintenance treatment. Current nebulizers are expensive, bulky, time-consuming to use and care for, and require maintenance. Furthermore, a nebulizer provides imprecise drug delivery unless equipped with a dosimeter. In infants and young children when even passive cooperation cannot be achieved, the loose face mask of a jet nebulizer is often more acceptable than the close-fitting face mask of a spacer. However, parents should be advised of the advantages of the MDI with spacer and encouraged to persevere with attempts at its use.

Controller Medications

Controller medications include inhaled glucocorticosteroids, systemic glucocorticosteroids, leukotriene modifiers, sodium cromoglycate (cromolyn sodium), nedocromil sodium, methylxanthines, long-acting inhaled beta2-agonists, and long-acting oral beta2-agonists. Inhaled glucocorticosteroids are at present the most effective controller medications. The evidence on the effects of ketotifen in children is insufficient to warrant its use. Details about these medications are provided in the original guideline document.

Reliever Medications

Details about these medications (beta2-agonists and anticholinergic agents) are provided in the original guideline document.

A Stepwise Approach to Pharmacologic Therapy

The stepwise treatment paradigm emphasizes that asthma at any age, even from early childhood, is a disease in which chronic airway inflammation underlies recurrent symptoms. Evidence suggests that any asthma more severe than intermittent is more effectively controlled by interventions that suppress and reverse this inflammation than by those that only treat the episodic bronchoconstriction and related symptoms.

The selection of pharmacologic treatment options is made on the basis of an individual patient's asthma severity, the patient's current treatment, the pharmacological properties and availability of various antiasthma treatments, and economic considerations. Because asthma is a dynamic as well as a chronic condition, medication plans must accommodate variability among patients as well as the variability of an individual patient's disease over time. An essential aspect of any treatment plan is monitoring of the effect of the treatment (including measurements of lung function and symptoms) and adaptation of the treatment to the variability of the asthma.

An approach to pharmacologic therapy in which treatment is correlated with asthma severity permits this flexibility. The classification of asthma severity should be made by means of evaluating the patient's symptoms, medical history, and current treatment, a clinical examination, and measurements of lung function where possible (see Figure 5-6, above, and Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document).

An appropriate approach to asthma therapy recommends that the number (type), dose, and eventually frequency of medications be increased with increasing asthma severity. The aim is to accomplish the goals of therapy with the least possible medication. In developing an asthma management plan, the health care professional must judge whether to give maximum treatment initially--which may involve a burst or cycle of oral glucocorticosteroids in order to achieve control of the patient's asthma as quickly as possible--and then decrease the medication, or to start with treatment judged appropriate for the severity of the patient's asthma and increase the treatment gradually if necessary. Once control of asthma is sustained for 3 months, a reduction in therapy can be carefully considered. This reduction in therapy is needed to identify the minimum therapy required to maintain control.

Figure 7-8, below, presents the stepwise approach to therapy to achieve and maintain control of asthma in children. The step system for classifying asthma severity takes into account the treatment that the patient is currently receiving (see Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document). Figure 7-8, below, presents all therapies that can be recommended for treating each step of asthma severity. Guidance for selecting among these available modalities is provided in the text of the original guideline document. The cost of the medication is an obvious factor in determining choice of treatment. Cost of treatment varies from country to country and is only one of the factors that contribute to the total cost of a disorder such as asthma.

Figure 7-8. Recommended Medications by Level of Severity: Children Younger Than 5 Years of Age

All Levels: In addition to daily controller therapy, a rapid-acting inhaled beta2-agonist* should be taken as needed to relieve symptoms, but should not be taken more than 3 to 4 times a day. Patient education is essential at every level.		
Level of Severity:**	Daily Controller Medications:	Other Treatment Options:***
Step 1. Intermittent asthma****	None necessary	
Step 2. Mild Persistent Asthma	Low-dose inhaled glucocorticosteroid (see original guideline document for dosage information)	• Sustained-release theophylline, OR • Cromone, OR • Leukotriene modifier
Step 3. Moderate Persistent Asthma	Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information)	• Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS sustained-release theophylline, OR • Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS long-acting oral beta2-agonist, OR • High-dose inhaled glucocorticosteroid (see original guideline document for dosage information), OR • Medium-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS leukotriene modifier
Step 4. Severe Persistent Asthma	High-dose inhaled glucocorticosteroid (see original guideline document for dosage information) PLUS long-acting inhaled beta2-agonist PLUS one or more of the following, if needed: • Sustained-release	

All Levels: In addition to daily controller therapy, a rapid-acting inhaled beta2-agonist* should be taken as needed to relieve symptoms, but should not be taken more than 3 to 4 times a day. Patient education is essential at every level.		
Level of Severity:**	Daily Controller Medications:	Other Treatment Options:***
	theophylline • Leukotriene modifier • Long-acting oral beta2-agonist • Oral glucocorticosteroid	
All Levels: Once control of asthma is achieved and maintained for at least three months, a gradual reduction of the maintenance therapy should be tried in order to identify the minimum therapy required to maintain control.		

* Other options for reliever medications are (in increasing order of cost) inhaled anticholinergic, short-acting oral beta2-agonist, and short-acting theophylline.
** See Figure 5-6, above, and Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document for classification of severity.
*** Other treatment options listed in order of increasing cost. Relative medication costs may vary from country to country.
**** Patients with intermittent asthma but severe exacerbations should be treated as having moderate persistent asthma (Evidence D).

How to Achieve and Maintain Control of Asthma

This section of the original guideline document describes the therapy appropriate for different steps of asthma severity. The presence of one or more features of clinical severity places a patient at the respective step (see Figure 5-6, above). The current treatment should be included in the assessment of severity (see Figure 5-7 titled "Classification of Asthma Severity by Daily Medication Regimen and Response to Treatment" in the original guideline document).

In the stepwise approach to therapy, progression to the next step is indicated when control is not achieved or is lost with the current treatment, and there is assurance the patient is using medication correctly. The frequent (e.g., more than 3 times a week) presence of such symptoms as cough, wheezing, and dyspnea, and the increased use of rapid-acting bronchodilators, may indicate inadequate control of asthma. The presence of symptoms at night or early in the morning is an especially useful indicator. Measurement of PEF and its variability is helpful in the initial assessment of asthma severity and in monitoring the initial treatment, assessing changes in severity, and preparing for a reduction in therapy.

The treatments suggested for each step are guidelines only. See the original guideline document for details. Specific medication plans should be tailored by the health care professional depending on the availability of antiasthma medication, the conditions of the health care system, and individual patient circumstances. Repeated use of reliever medication more than 4 times a day indicates that the patient's asthma is not well controlled, and the intensity of treatment should be increased.

Preschool children and infants. Although there are no well-conducted clinical trials to provide scientific evidence for the proper treatment of asthma at each step of severity in these age groups, a treatment algorithm similar to that used in school children is recommended for preschool children and infants. Some adjustments must be made to account for the fact that in these younger children it is difficult to predict the need for reliever medications. At this age, children rarely communicate a need for reliever treatment, and caregivers are often unaware of the signals to observe and are unfamiliar with the drug treatment. These considerations argue for early introduction of controller treatment rather than reliance on "as-needed" rescue treatment. Preschool children and infants with wheeze represent a more heterogeneous group than school children. Thus, the specificity of the asthma diagnosis in children under 3 is poor, and aerosol treatment may present an obstacle to regular treatment.

Young children with asthma may be hospitalized with severe symptoms related to an upper airway infection. Courses of inhaled or oral glucocorticosteroids during such infections may reduce duration and severity of exacerbations, but there is no current evidence to support low-dose maintenance therapy with inhaled glucocorticosteroids in children younger than 3.

Part 5: Establish Plans for Managing Exacerbations

Key Points

- Treatment of exacerbations depends on the patient, experience of the health care professional, therapies that are most effective for the particular patient, availability of medications, and emergency facilities.
- Primary therapies for exacerbations are the repetitive administration of rapid-acting inhaled beta2-agonist, the early introduction of systemic glucocorticosteroids, and oxygen supplementation.
- Crucial to successful treatment of exacerbations is close monitoring of the patient's condition and response to treatment with serial measurements of lung function.
- Severe exacerbations of asthma are life-threatening medical emergencies. Care must be expeditious, and treatment is often most safely undertaken in a hospital or a hospital-based emergency department.

The primary therapies for exacerbations are the repetitive administration of rapid-acting inhaled beta2-agonist, the early introduction of systemic glucocorticosteroids, and oxygen supplementation. The aims of treatment are to relieve airflow obstruction and hypoxemia as quickly as possible, and to plan the prevention of future relapses. Crucial to successful treatment is close monitoring of the patient's condition and response to treatment with serial measurements of lung function. Assessment of the patient's pulse, respiratory rate, and current symptoms also guides treatment decisions, but measurements of lung function and oximetry are critical.

Patients at high risk of asthma-related death require prompt care, particularly close monitoring, and intensive patient education. These patients include those:

- With a history of near-fatal asthma requiring intubation and mechanical ventilation, which puts patients at a 19-fold increased risk of needing intubation during subsequent exacerbations
- Who have had a hospitalization or emergency care visit for asthma in the past year
- Who are currently using or have recently stopped using oral glucocorticosteroids
- Who are not currently using inhaled glucocorticosteroids, which appear to offer a protective effect against death or near-fatal asthma
- Who are over-dependent on rapid-acting inhaled beta2-agonists, especially those who use more than one canister of salbutamol (or equivalent) monthly
- With a history of psychiatric disease or psychosocial problems, including the use of sedatives
- With a history of noncompliance with an asthma medication plan

Full recovery from asthma exacerbations is usually gradual. It may take many days for lung function to return to normal and weeks for airway hyperresponsiveness to decrease. Symptoms and physical signs are not accurate indicators of airflow limitation. The increased treatment should continue until measurements of lung function (PEF or FEV_1) return close to normal, or the patient's personal best.

Assessment of Severity of the Exacerbation

The severity of the exacerbation determines the treatment administered. Figure 7-9 titled "Severity of Asthma Exacerbations" in the original guideline document provides a guide to the severity of an exacerbation of asthma at the time the examination is made. Because these are guidelines only, all features in a category need not be present. A more severe grading should be given if the patient has a lack of response to initial treatment, if the exacerbation has progressed quickly, or if the patient is at high risk for asthma-related death.

Indices of severity, particularly PEF (in patients over 5 years old), pulse, respiratory rate, and pulse oximetry (in children) should be monitored during treatment. Any deterioration may require prompt intervention. Pulse oximetry has been shown to be particularly useful in pediatric acute asthma. Data also suggest that there are important differences in PEF patterns between periods of poor asthma control and exacerbations; in one study PEF fell during exacerbations, but there was less diurnal variation during exacerbations than during periods of poor asthma control.

Home Management of Exacerbations

Initiation of appropriate therapy at the earliest possible signs of deteriorating control of asthma is important in the successful management of asthma exacerbations. When patients are able to begin treatment at home, they not only avoid delays in treatment but also add to their sense of control over their asthma. The degree of care provided in the home depends on the health care professional's and patient's (or parents') experience and the availability of medications and emergency care. Figure 7-10 titled "Management of Asthma Exacerbations" in the original guideline document illustrates the approach to home treatment.

Home PEF measurements ideally should be an integral part of home management strategies, although the degree of symptoms is a more sensitive detector of the early stages of an asthma attack than is PEF. Ideally, all patients should have a written action plan with both a symptom and a peak flow component that outlines how and when to:

- Recognize signs of deterioration
- Modify or augment treatment
- Assess the severity of the attack
- Obtain more specialized care if appropriate

Treatment

Bronchodilators. For moderate exacerbations, repeated administration of rapid-acting inhaled beta2-agonists (2 to 4 puffs every 20 minutes for the first hour) is usually the best and most cost-effective method to achieve rapid reversal of airflow limitation. After the first hour, the dose of beta2-agonist required will depend on the severity of the exacerbation. Mild exacerbations respond 2 to 4 puffs every 3 to 4 hours; moderate exacerbations will require 6 to 10 puffs every 1 or 2 hours; for more severe exacerbations, up to 10 puffs (preferably given with a spacer), or full doses given via nebulizer, may be required at less than hourly intervals. Bronchodilator therapy delivered via an MDI, ideally with a spacer, produces at least an equivalent improvement in lung function as the same dose delivered via nebulizer. Depending upon the proportion of patients able to use an MDI, this route of delivery is also likely to be more cost effective. No additional medication is necessary if the rapid-acting inhaled beta2-agonist produces a complete response (PEF returns to greater than 80 percent of predicted or personal best) and the response lasts at least 3 to 4 hours.

Glucocorticosteroids. A number of studies indicate a benefit from action plans that integrate an increase in inhaled glucocorticosteroids early in an asthma exacerbation. The data to support the utility of this strategy are limited.

Oral glucocorticosteroids (0.5 to 1 mg/kg prednisolone or equivalent during a 24-hour period) should be used to speed resolution of all but the mildest exacerbations. A useful rough guide is to use oral glucocorticosteroids if the response to the rapid-acting inhaled beta2-agonist alone is not prompt or sustained (e.g., PEF greater than 80 percent of predicted or personal best) after 1 hour.

Additional Care

If there is sustained improvement in PEF and symptoms, care may be continued at home under supervision. Full recovery from the exacerbation is often gradual, and medications for the exacerbation may need to be continued for several days to sustain relief of symptoms and improvement in PEF.

There should be no delay in seeking medical help if:

- The patient is at a high risk for asthma-related death

- The exacerbation is severe (e.g., PEF remains less than 60 percent of predicted or personal best after beta2-agonist therapy)
- The response to the bronchodilator is not prompt and sustained for at least 3 hours
- There is no improvement within 2 to 6 hours after glucocorticosteroid treatment is started
- There is further deterioration

Hospital-Based Management of Exacerbations

Severe exacerbations of asthma are life-threatening medical emergencies. Care must be expeditious, and treatment is often most safely undertaken in a hospital or a hospital-based emergency department. Figure 7-11 titled "Hospital-Based Management of Asthma Exacerbations" in the original guideline document illustrates the approach to hospital-based management of exacerbations.

Assessment

A brief history and physical examination pertinent to the exacerbation should be conducted concurrently with the prompt initiation of therapy. Laboratory studies should not be permitted to delay initiation of treatment.

The brief history should include: severity of symptoms, including exercise limitation and sleep disturbance; all current medication, including dose (and device) prescribed, dose usually taken, dose taken in response to the deterioration, and the patient's response (or lack thereof) to this therapy; time of onset and cause of the present exacerbation; and risk factors for asthma-related death, especially prior hospitalizations, intensive care admission, and emergency department visits for asthma.

The physical examination should assess the severity of the exacerbation (by evaluating the patient's ability to complete a sentence, pulse rate, respiratory rate, pulsus paradoxicus [though this is a very imprecise sign in children], use of accessory muscles, and other signs detailed in Figure 7-11 titled "Hospital-Based Management of Asthma Exacerbations" in the original guideline document) and identify complications (e.g., pneumonia, atelectasis, pneumothorax, or pneumomediastinum).

Functional assessments include PEF or FEV_1 and arterial oxygen saturation measurements. A baseline PEF or FEV_1 measurement should be made before treatment is initiated, if possible, without unduly delaying treatment. Subsequent measurements should be made at intervals until a clear response to treatment has occurred.

Oxygen saturation should be closely monitored, preferably by pulse oximetry. This is especially useful in children because objective measurements of lung function may be difficult and an oxygen saturation less than 92 percent is a good predictor of the need for hospitalization (Evidence C).

After initial treatment, a chest x-ray and arterial blood gas measurements may be helpful in some patients. In adults a chest x-ray is not routinely required, but

should be carried out if a complicating cardiopulmonary process is suspected, in patients requiring hospitalization, and in those not responding to treatment where a pneumothorax may be difficult to diagnose clinically. Similarly, in children, routine chest x-rays are not recommended unless there are physical signs suggestive of parenchymal disease (Evidence C).

Arterial blood gas measurements are not routinely required, but should be completed in patients with a PEF of 30 to 50 percent predicted and those who do not respond to initial treatment. The patient should continue on supplemental oxygen while the measurement is made. A partial pressure of arterial oxygen PaO_2 less than 60 mm Hg (8 kPa) and a normal or increased partial pressure of arterial carbon dioxide ($PaCO_2$) (especially greater than 45 mm Hg, 6 kPa) indicates the potential for or presence of respiratory failure. In these circumstances stabilization of the patient in a monitored area, and in the absence of improvement admission to an intensive care unit for ongoing care, is recommended (Evidence D).

Special considerations for infants and young children. Several differences in lung anatomy and physiology place infants at theoretically greater risk than older children for respiratory failure. Despite this, respiratory failure is rare in infancy. Close monitoring, using a combination of the parameters listed in Figure 7-9 titled "Severity of Asthma Exacerbations" in the original guideline document other than PEF, will permit a fairly accurate assessment. Breathlessness sufficiently severe to prevent feeding is an important symptom of impending respiratory failure.

Oxygen saturation, which should be measured in infants by pulse oximetry, is normally greater than 95 percent. Arterial or arterialized capillary blood gas measurement should be considered in infants with oxygen saturation less than 90 percent on high-flow oxygen whose condition is deteriorating.

Treatment

The following treatments are usually administered concurrently to achieve the most rapid resolution of the exacerbation.

Oxygen. To achieve arterial oxygen saturation of greater than or equal to 90 percent (95 percent in children), oxygen should be administered by nasal cannulae, by mask, or rarely by head box in some infants. Supplemental oxygen should be administered to patients when arterial oxygen monitoring is not available. One study suggests that $PaCO_2$ may worsen in some patients on 100 percent oxygen, especially those with more severe airflow obstruction. Oxygen therapy should be titrated against pulse oximetry to maintain satisfactory oxygen saturation (greater than 92%).

Rapid-acting inhaled beta2-agonists. Although rapid-acting inhaled beta2-agonists are generally administered by nebulization, equivalent bronchodilatation with a more rapid onset, fewer side effects, and less time in the emergency department can be achieved using an MDI with a spacer (Evidence A). However, for some children, administration by nebulizer may be easier. If a jet nebulizer is used, it should be driven by oxygen instead of air. Preliminary results indicate that if salbutamol is used, it may provide greater benefit if it is administered in isotonic magnesium sulfate than in normal saline (Evidence B), although isotonic

magnesium sulfate cannot be routinely recommended until further studies are complete. Although therapy should ideally be given by the inhaled route, if inhaled medications are not available then oral bronchodilators may be considered. Although short-acting beta2-agonists are the recommended treatment in acute asthma, the long-acting bronchodilator, formoterol, which has rapid onset of action, was shown to be equivalent without increasing side effects, but is considerably more expensive.

Compared to racemic albuterol, a modest additional bronchodilator effect has been shown with levalbuterol. However, there is a substantially higher cost to this therapy which does not support its use in stable asthma. In a large pediatric acute asthma study, levalbuterol treatment reduced hospitalization rates compared to the racemic albuterol treatment group, but length of hospital stay was no different between groups.

Studies of intermittent versus continuous nebulized short-acting beta2-agonists, in acute asthma, provide conflicting results. In a systematic review of six studies, there were no significant differences in bronchodilator effect or in admissions to hospital between the two groups. In two of the six studies, continuous treatment was associated with a lower heart rate and less fall in serum potassium. Thus, overall there may be marginal safety benefit to the use of continuous versus intermittent therapy, although it is unclear if this is clinically significant. In patients who do require hospitalization, one study found that on-demand therapy led to a significantly shorter hospital stay, fewer nebulizations, and fewer palpitations when compared with regular therapy given every 4 hours. A reasonable approach to inhaled therapy in exacerbations, therefore, would be the initial use of continuous therapy, followed by on-demand therapy for hospitalized patients.

There is no evidence to support the use of intravenous B2-agonists in patients with severe asthma who are treated with nebulized B2-agonists.

Epinephrine. A subcutaneous or intramuscular injection of epinephrine (adrenaline) may be indicated for acute treatment of anaphylaxis and angioedema. Epinephrine can be used in the treatment of severe acute exacerbations of asthma if beta2-agonists (inhaled or parenteral) are not available. However, the possibility of adverse effects, particularly among hypoxic patients, is greater. Although epinephrine is sometimes considered if a severe acute exacerbation is not responsive to rapid-acting inhaled beta2-agonist, a more logical approach, based upon the above data, would be to add an intravenous beta2-agonist (Evidence B).

Additional Bronchodilators

Ipratropium bromide. A combination of nebulized beta2-agonist with an anticholinergic (ipratropium bromide) may produce better bronchodilation than either drug alone (Evidence B), and should be administered before methylxanthines are considered. A number of studies indicate that combination therapy is associated with lower hospitalization rates (Evidence A) and greater improvement in PEF and FEV_1 (Evidence B). Similar data have been reported in the pediatric literature (Evidence A). However, once hospitalized, the addition of nebulized ipratropium bromide to nebulized B2-agonist and systemic

glucocorticoids appears to confer no extra benefit to children with asthma hospitalized following intensive emergency department treatment.

Methylxanthines. Methylxanthines have equivalent bronchodilator effect to inhaled beta2-agonists, but because of increased side effects, methylxanthines should only be considered as an alternate therapy. In one study in children with near fatal asthma, intravenous methylxanthines appear to add benefit to those also receiving an aggressive regimen of inhaled and intravenous beta2-agonists, inhaled ipratropium bromide, and intravenous systemic glucocorticosteroids.

Systemic glucocorticosteroids. Systemic glucocorticosteroids speed resolution of exacerbations and should be considered integral to the management of all but the mildest (see Figure 7-9 titled "Severity of Asthma Exacerbations" in the original guideline document) exacerbations (Evidence A) especially if:

- The initial rapid-acting inhaled beta2-agonist dose has failed to achieve lasting improvement
- The exacerbation developed even though the patient was already taking oral glucocorticosteroids
- Previous exacerbations required oral glucocorticosteroids

Systemic glucocorticosteroids administered by ingestion are usually as effective as those administered intravenously and are preferred because this route of delivery is less invasive and less expensive. If vomiting has occurred shortly after administration of the oral dose of glucocorticosteroids, then a similar dose should be readministered. Intravenous administration may be considered if intravenous access is desirable, or if there is possible impairment of gastrointestinal absorption. In patients being discharged from the emergency department, intramuscular administration may be helpful, especially if there are concerns about compliance.

Systemic glucocorticosteroids require at least 4 hours to produce clinical improvement. A meta-analysis has suggested that doses of systemic glucocorticosteroids equivalent to 60 to 80 mg methylprednisolone or 300 to 400 mg hydrocortisone per day are adequate for hospitalized patients, and even 40 mg methylprednisolone or 200 mg hydrocortisone is probably adequate (Evidence B). There are no convincing data on the proper duration of oral prednisone treatment, although a 10- to 14-day course in adults and a 3- to 5-day course in children is usually considered appropriate (Evidence D). Current evidence suggests that there is no benefit to tapering the dose of oral prednisone either in the short term or over several weeks (Evidence B).

Inhaled glucocorticosteroids. The optimum increase in maintenance inhaled glucocorticosteroids to prevent an asthma exacerbation is not well defined. Previous guidelines have recommended doubling the dose of inhaled glucocorticosteroids, but there is no evidence to support this recommendation. Higher doses may be appropriate.

Inhaled glucocorticosteroids are effective as part of combination therapy for asthma exacerbations that have already developed. One study has shown that the combination of high-dose inhaled glucocorticosteroids and salbutamol in acute asthma provides greater bronchodilation than salbutamol alone (Evidence B). In

addition, inhaled glucocorticosteroids can be as effective as oral glucocorticosteroids at preventing relapses. Patients discharged from the emergency department on prednisone and inhaled budesonide have a lower rate of relapse than those on prednisone alone (Evidence B). A high dose of inhaled glucocorticosteroids (2.4 mg budesonide daily in 4 divided doses) achieves a relapse rate similar to 40 mg oral prednisone daily (Evidence A). Although cost is a major factor in using inhaled glucocorticosteroids as adjunct therapy, these studies indicate that in patients intolerant of or not willing to take oral prednisone, similar results can be achieved with very high doses of inhaled glucocorticosteroids. Further studies are required to document the potential benefits of inhaled glucocorticosteroids in acute asthma. This is especially important given the cost effectiveness of a short course of oral prednisone.

Magnesium. Present evidence suggests that intravenous magnesium should not be used routinely in asthma exacerbations but can help reduce hospital admission rates in selected groups of patients: adults with FEV_1 25 to 30 percent predicted at presentation; adults and children who fail to respond to initial treatment; and children whose FEV_1 fails to improve above 60 percent predicted after 1 hour of care (Evidence A). Intravenous magnesium is usually given as a single 2-g infusion over 20 minutes. No additional monitoring is required and there are no reported side effects. One study indicated that use of isotonic magnesium as an adjuvant to nebulized salbutamol results in an enhanced bronchodilator response in treatment of severe asthma. Before this therapy is routinely used further studies are needed.

Helium oxygen therapy. Studies that have evaluated the effect of a combination of helium and oxygen (heliox), compared to oxygen alone, on airflow obstruction and dyspnea suggest that this treatment should not be used routinely for mild to moderate asthma (Evidence B), but should be reserved for patients with more severe disease (Evidence B). The role of heliox for the treatment of moderate to severe asthma in emergency department patients is uncertain.

Other Treatments

- Antibiotics are not routinely required unless there are signs of pneumonia or fever and purulent sputum suggesting bacterial infection, especially if bacterial sinusitis is suspected.
- Inhaled mucolytic drugs have not been shown to benefit treatment of exacerbations, and in severe exacerbations they may worsen cough or airflow limitation.
- Sedation should be strictly avoided during exacerbations of asthma because of the respiratory depressant effect of anxiolytic and hypnotic drugs. Studies show an association between the use of these drugs and avoidable asthma deaths.
- Antihistamines and chest physical therapy have no established role in the treatment of exacerbations.

Special considerations for infants and young children. Attention to fluid balance may be necessary for infants and young children, who may become dehydrated as a result of increased respiratory rates and with decreased oral intakes during an exacerbation. When treatments offer similar profiles for efficacy and safety, noninvasive procedures are preferred in order to avoid pain and anxiety. Thus

inhaled beta2-agonist (delivered by mouthpiece) and oral glucocorticosteroid therapy are preferred to intravenous or subcutaneous therapy, and pulse oximetry is preferred to arterial blood gas measurements.

Criteria for Continuous Monitoring

Factors indicating the need for close and continuous supervision that is provided either in a hospital or dispensary, depending on available facilities, include:

- Inadequate or deteriorating response to therapy within 1 to 2 hours of treatment
- Persisting severe airflow limitation (PEF less than 30 percent of predicted or personal best)
- Past history of severe asthma, particularly if hospitalization and admission to the intensive care unit was required
- Presence of factors indicating high risk of asthma-related death
- Prolonged symptoms before the current emergency department visit
- Inadequate access at home to medical care and medications
- Difficult home conditions
- Difficulty obtaining transport to hospital in the event of further deterioration.

See the original guideline document for criteria for discharge from emergency department versus hospitalization, criteria for admission to intensive care unit, discharge from emergency department, and discharge from continuous supervision.

Part 6: Provide Regular Follow-Up Care

Patients with asthma need regular supervision and support by a health care professional who is knowledgeable about the condition. Continual monitoring is essential to assure that therapeutic goals are met.

While the patient is achieving control of asthma, frequent follow-up visits are necessary to review home PEF and symptom records, the techniques in using medication, risk factors and methods to control them.

Consultation with an asthma specialist is recommended under certain circumstances when:

- The patient has had a life-threatening asthma exacerbation, has poor self-management ability, or has difficult family dynamics.
- Signs and symptoms are atypical or there are problems in differential diagnosis.
- Clinical entities complicate asthma (e.g., sinusitis, nasal polyps, aspergillosis, severe rhinitis).
- Additional diagnostic testing is indicated (e.g., skin testing, rhinoscopy, complete pulmonary function studies, provocative studies).
- The patient is not responding optimally to the asthma therapy.
- The patient requires Step 3 or 4 care (moderate persistent to severe persistent asthma) to control asthma.

- The patient requires guidance on environmental control, consideration of immunotherapy, smoking cessation, complications of therapy, or difficult compliance issues.

Once control is established, regular follow-up visits (at 1- to 6-month intervals as appropriate) continue to be essential. Health care professionals need to monitor and review the treatment plans, the medications, the patient's management techniques (e.g., for using medicines and peak flow meters, for controlling the environment), and the level of asthma control (PEF and symptom reports). The most appropriate method for follow-up will depend on the health care system. A patient visit to a primary health care or specialist office, an outreach worker visit to patient homes, or follow-up for asthma that is integrated with a visit for another reason (well care, an acute illness other than asthma) can each be a suitable means for providing the ongoing care essential for control of this chronic disorder.

The following special considerations are considered in the original guideline document: pregnancy; surgery; physical activity; rhinitis, sinusitis, and nasal polyps; occupational asthma; respiratory infections; gastroesophageal reflux; aspirin-induced asthma, and anaphylaxis and asthma.

Definitions:

Description of Levels of Evidence:

A. Randomized controlled trials. Rich body of data.
   Definition: Evidence is from endpoints of well-designed randomized controlled trials that provide a consistent pattern of findings in the population for which the recommendation is made. Category A requires substantial numbers of studies involving substantial numbers of participants.
B. Randomized controlled trials. Limited data.
   Definition: Evidence is from endpoints of intervention studies that include only a limited number of patients, post hoc or subgroup analysis of randomized controlled trials, or meta-analysis of randomized controlled trials. In general, Category B pertains when few randomized trials exist, they are small in size, they were undertaken in a population that differs from the target population of the recommendation, or the results are somewhat inconsistent.
C. Nonrandomized trials. Observational studies.
   Definition: Evidence is from outcomes of uncontrolled or nonrandomized trials or from observational studies.
D. Panel consensus judgment.
   Definition: This category is used only in cases where the provision of some guidance was deemed valuable but the clinical literature addressing the subject was insufficient to justify placement in one of the other categories. The Panel Consensus is based on clinical experience or knowledge that does not meet the above-listed criteria.

Abbreviations:

- ACE, angiotensin-converting enzyme inhibitors
- CFC, chlorofluorocarbon(s)
- CO, carbon monoxide

- COPD, chronic obstructive pulmonary disease
- DPI, dry powder inhaler
- ECG, electrocardiogram
- FEV_1, forced expiratory volume in one second
- FVC, forced vital capacity
- GINA, Global Initiative for Asthma
- HFA, hydrofluoroalkanes
- IgE, Immune globulin E
- MDI, metered-dose inhaler
- NO, nitrous oxide
- $PaCO_2$, partial pressure of arterial carbon dioxide
- PaO_2, partial pressure of arterial oxygen
- PEF, peak expiratory flow

CLINICAL ALGORITHM(S)

Algorithms are provided in the original guideline document for:

- Differential diagnosis of obstructive airway diseases
- Management of exacerbation of asthma: home-treatment
- Hospital-based management of asthma exacerbations

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for select recommendations (see Major Recommendations).

Levels of evidence are assigned to management recommendations in the Global Initiative for Asthma (GINA) documents were appropriate in Chapter 6, "Education and Delivery of Care," and Chapter 7, "A Six-Part Asthma Management Program," and are indicated in boldface type enclosed in parentheses after the relevant statement--e.g., (Evidence A). However, evidence may not be available for all recommendations and, in this case, is clearly labeled as "expert opinion," (Evidence D). The methodological issues concerning the use of evidence from meta-analyses were carefully considered (e.g., a meta-analysis of a number of smaller studies was considered to be evidence level B).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Asthma is a chronic disorder with significant impact on individuals, their families, and society. Although there is no cure for asthma, appropriate diagnosis and management most often leads to control of the disorder. The goals for successful management of asthma are to:

- Achieve and maintain control of symptoms
- Prevent asthma exacerbations

- Maintain pulmonary function as close to normal levels as possible
- Maintain normal activity levels, including exercise
- Avoid adverse effects from asthma medications
- Prevent development of irreversible airflow limitation
- Prevent asthma mortality

Patient education is an essential component of asthma care. An aim is for the patient to be offered training in self-management techniques. A recent systematic review by the Cochrane Airways group of 22 studies involving patient education compared with usual care showed significant benefits in the intervention groups in terms of reduced morbidity and reduced use of health services. The effects were greatest where the intervention involved the issuing of written self-management action plans.

Subgroups Most Likely to Benefit

Infants: Avoidance of passive smoke, especially by infants, is very likely to be beneficial.

POTENTIAL HARMS

Side Effects of Medications:

Controller (Long-term Preventive) Medications

- Inhaled corticosteroids: Local adverse effects from inhaled corticosteroids include oropharyngeal candidiasis, dysphonia, and occasional coughing from upper airway irritation. These effects may be prevented by use of spacer devices, gargling with (and spitting out) water, or gargling with a one part per fifty (1:50) dilution of amphotericin B.
- Cromones (e.g., sodium cromoglycate): Minimal side effects include cough upon inhalation.
- Systemic corticosteroids: Long-term use may produce systemic effects including osteoporosis and fractures, arterial hypertension, diabetes, hypothalamic-pituitary-adrenal axis suppression, cataracts, glaucoma, obesity, skin thinning leading to cutaneous striae and easy bruisability, and muscle weakness.
- Theophylline: Sustained-release theophylline has the potential for significant adverse effects. The signs and symptoms of theophylline intoxication involve many different organ systems. Gastrointestinal symptoms, nausea, and vomiting are the most common early events. Theophylline intoxication can result in seizures and even death, and these events may not be preceded by evidence of central nervous system stimulation. Cardiopulmonary effects include tachycardia, arrhythmias, and occasionally, stimulation of the respiratory center.
- Beta2-agonists: Long-acting inhaled beta2-agonists are associated with systemic adverse effects (although fewer than oral therapy) such as cardiovascular stimulation, skeletal muscle tremor, anxiety, pyrosis, headache, and hypokalemia. Long-acting oral beta2-agonists may cause cardiovascular stimulation, anxiety, pyrosis, skeletal muscle tremor.
- Ketotifen: The most frequent side effect is sedation, especially in the initial treatment period and in adults. Ketotifen may also cause weight gain.

- Antileukotrienes: Elevation of liver enzymes is possible. Limited case reports of reversible hepatitis and hyperbilirubinemia exist. There are several reports of Churg-Strauss syndrome in association with leukotriene modifier therapy.
- Second-generation antihistamines: The most frequent side effect is sedation, especially in the initial treatment period.
- Systemic steroid-sparing therapies: Side effects vary with the medication, but commonly include nausea, vomiting, and abdominal pain. Less frequent but potentially severe adverse effects include hepatitis and hematological, teratogenic, and pulmonary effects.
- Specific immunotherapy (SIT): Local and systemic side effects may occur in conjunction with administration. Reactions localized to the injection site may range from a minimal immediate wheal and flare to a large, painful, delayed allergic response. Systemic effects may include anaphylactic reactions, which may be life threatening, as well as severe exacerbations of asthma.

Reliever (Quick-relief) Medications

- Beta2-agonists: Short-acting inhaled beta2-agonists may cause systemic adverse effects (although fewer than oral therapy) such as cardiovascular stimulation, skeletal muscle tremor, and hypokalemia. Oral beta2-agonists are associated with the potential for cardiovascular stimulation, skeletal muscle tremor, hypokalemia, and irritability.
- Systemic corticosteroids: Potential side effects of high-dose short-term systemic therapy include reversible abnormalities in glucose metabolism; increased appetite; fluid retention; weight gain; rounding of the face; mood alteration; hypertension; peptic ulcer; and aseptic necrosis of the femur. These effects are generally not observed during a short course of oral or parenteral therapy.
- Anticholinergics: Inhalation of ipratropium or oxitropium can cause a dryness of the mouth and a bad taste.
- Short-acting theophylline: Theophylline has the potential for significant adverse effects. The signs and symptoms of theophylline intoxication involve many different organ systems. Gastrointestinal symptoms, nausea, and vomiting are the most common early events. Theophylline intoxication can result in seizures and even death. Cardiopulmonary effects include tachycardia, arrhythmias, and occasionally, stimulation of the respiratory center.
- Epinephrine/adrenaline: Epinephrine/adrenaline injection is associated with similar, but more significant effects than beta2-agonist. In addition, convulsions, chills, fever, and hallucinations may occur.

<u>Subgroups Most Likely to Be Harmed</u>

- Children and inhaled corticosteroids: Minor growth delay or suppression (average 1 cm) may occur in children
- Comorbid conditions and systemic corticosteroids: Caution and close medical supervision are recommended when considering the use of systemic corticosteroids in patients with asthma who also have tuberculosis, parasitic infections, osteoporosis, glaucoma, hypertension, diabetes, severe depression, or peptic ulcers. Fatal herpes virus infections have been reported among patients who are exposed to these viruses while taking systemic corticosteroids, even short bursts

- Theophylline: Monitoring patients is advised when conditions known to alter theophylline metabolism exist (e.g., febrile illness, pregnancy, liver disease, congestive heart failure, and the use of certain drugs, including cimetidine, certain quinolones, and certain macrolides)
- Combination therapy: Adverse cardiovascular reactions may occur with the combination of oral beta2-agonists and theophylline

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The recommended treatments outlined in the guideline are guidelines only. Local resources and individual circumstances determine specific therapy.
- It is recognized that a large segment of the world's population lives in areas with inadequate medical facilities and meager financial resources. It is also recognized that "fixed" international guidelines and "rigid" scientific protocols will not work in many locations. Thus, the Global Initiative for Asthma (GINA) Committees encourage that recommendations found in this Report be adapted to fit local practices and the availability of health care resources.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

While the guideline outlines specific recommendations for clinical management of asthma, regional and national health care planners and health authorities need to develop specific strategies for implementing the recommendations.

The following conditions are essential to effective asthma care delivery:

- Sufficient numbers of well-educated health professionals should be organized effectively so that they are available to the maximum number of patients.
- Asthma should be correctly diagnosed, its severity assessed, and appropriate treatments prescribed.
- Adequate finances should be available to governments or individuals to ensure that asthma treatments are available (and means of providing less expensive medications need to be explored).
- Patients should understand how to use the asthma treatments to maximal advantage.

See Chapter 6, "Education and the Delivery of Care" in the original guideline document for further information on strategies for implementation.

The Global Initiative for Asthma (GINA) Executive Committee has formed a Dissemination Committee * to enhance communication with asthma specialists, primary-care health professionals, other health care workers, and patient support organizations. The Committee will also examine barriers to implementation of the recommendations in this Report, especially the challenges that arise in primary-care settings and in developing countries.

*The Dissemination Committee was replaced in 2004 with a GINA Assembly to assure inclusion of a large number of participants from many countries.

The GINA program has developed a network of individuals who care for asthma patients in many different health care settings, including many developing countries. Many of these individuals were invited to serve on the GINA Assembly. Members of the GINA Assembly meet at least twice each year. While the members of the GINA committees acknowledge that early diagnosis of asthma and implementation of appropriate therapy significantly reduce the socioeconomic burdens of asthma and enhance patients' quality of life, many emphasize that medications continue to be the major component of the cost of asthma treatment. They urge that the pricing of asthma medications continue to be examined, as this has important implications for the overall costs of asthma management.

It is recognized that a large segment of the world's population lives in areas with inadequate medical facilities and meager financial resources. It is also recognized that "fixed" international guidelines and "rigid" scientific protocols will not work in many locations. Thus, the GINA Committees encourage that recommendations found in this Report be adapted to fit local practices and the availability of health care resources.

As the GINA Committees expand their work, every effort will be made to interact with patient and physician groups at national, district, and local levels, and in multiple health care settings, to continuously examine new and innovative approaches that will ensure the delivery of the best asthma care possible.

IMPLEMENTATION TOOLS

Clinical Algorithm
Foreign Language Translations
Patient Resources
Pocket Guide/Reference Cards
Slide Presentation

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2005. 184 p. [1372 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1995 Jan (revised 2005)

GUIDELINE DEVELOPER(S)

National Heart, Lung, and Blood Institute (U.S.) - Federal Government Agency [U.S.]
World Health Organization - International Agency

GUIDELINE DEVELOPER COMMENT

The Global Initiative for Asthma (GINA) is a collaborative project of the U.S. National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO).

SOURCE(S) OF FUNDING

The Global Initiative for Asthma (GINA) has been made possible by educational grants from: Altana, Andi-Ventis, AstraZeneca, Aventis, Bayer, Boehringer Ingelheim, Chiesi Group, GlaxoSmithKline, Merck, Sharp & Dohme, Mitsubishi-Pharma Corporation, Nikken Chemicals Co., LTD., Novartis, Schering-Plough International, and Viatris.

GUIDELINE COMMITTEE

Global Strategy for Asthma Management and Prevention National Heart, Lung and Blood Institute (NHLBI)/World Health Organization (WHO) Workshop

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Global Initiative for Asthma (GINA) Executive Committee Members (updated 2004): Paul O'Byrne, MD, Chair, McMaster University, Hamilton, Ontario, Canada; Eric D. Bateman, MD, University of Cape Town, Cape Town, South Africa; Jean Bousquet, M.D., PhD, Montpellier University/INSERM, Montpellier, France; William W. Busse, MD, University of Wisconsin, Madison, Wisconsin, USA; T.J.H. Clark, MD, Imperial College, London, UK; Ken Ohta. MD, Teikyo University School of

Medicine, Tokyo, Japan; Pierluigi Paggiaro, MD, University of Pisa, Pisa, Italy; Soren Erik Pedersen, MD, Kolding Hospital, Kolding, Denmark; Raj B Singh MD, Apollo Hospital, Chennai, India; Manuel Soto-Quiroz, MD, University of Costa Rica, San Jose, Costa Rica; Wan-Cheng Tan, MD, St Paul's Hospital, Vancouver, BC, Canada

Members of the Science Committee: Eric D. Bateman, MD; Peter J. Barnes, DM, DSc; Jean Bousquet, MD, PhD; William W. Busse, MD; Jeffery M, Drazen, MD; J. Mark FitzGerald, MD; Peter Gibson, MD; Paul O'Byrne, MD (Chair); Ken Ohta, MD; Soren Erik Pedersen, MD; Emilio Pizzichini, MD; Sean D. Sullivan, PhD; Sally E. Wenzel, MD; Heather J. Zar, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

ENDORSER(S)

American Academy of Allergy, Asthma and Immunology - Medical Specialty Society
American Thoracic Society - Medical Specialty Society
Asthma and Bronchitis Association of India - Disease Specific Society
China Allergy Society - Disease Specific Society
Chinese Preventive Medical Association - Medical Specialty Society
Chinese Thoracic Society - Medical Specialty Society
European Academy of Allergy and Clinical Immunology - Medical Specialty Society
European Respiratory Society - Professional Association
French Society of Allergy and Immunology (Societe Francaise d'Allergologie et d'Immunologie) - Medical Specialty Society
Georgian Association of Allergology - Medical Specialty Society
Indian Academy of Allergy - Medical Specialty Society
Indian Chest Society - Medical Specialty Society
Indonesian Asthma Foundation - Disease Specific Society
Interasthma - Disease Specific Society
Japanese Society of Allergology - Medical Specialty Society
Japanese Society of Pediatric Allergy - Medical Specialty Society
Latin American Society of Allergy and Immunology - Medical Specialty Society
Latin American Society of Pediatrics - Medical Specialty Society
Union Latinoamericana de Sociadades de Tisiologia y Enfermedades Respiratorias - Medical Specialty Society

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI). Global strategy for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma (GINA), National Heart, Lung and Blood Institute (NHLBI); 2004. 182 p.

In an effort to keep the GINA Workshop report as up to date as possible, a GINA Science Committee has been established to review published research on asthma management and prevention, and to post yearly updates on the GINA Web site. See the GINA Web site for archived versions of the GINA guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Global Initiative for Asthma (GINA) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Asthma management and prevention. A practical guide for public health officials and health care professionals. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 1995 Dec. Electronic copies available from the Global Initiative for Asthma Web site.
- Pocket guide for asthma management and prevention. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2005. Electronic copies available from the Global Initiative for Asthma Web site.
- Pocket guide for asthma management and prevention in children. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2005. Electronic copies available from the Global Initiative for Asthma Web site.
- Teaching slide set: global initiative for asthma. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2004. Electronic copies available from the Global Initiative for Asthma Web site.
- Dissemination and implementation of asthma guidelines. Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 2003. Electronic copies available from the Global Initiative for Asthma Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France.

PATIENT RESOURCES

The following is available:

- Patient care information booklet: what you and your family can do about asthma? Bethesda (MD): Global Initiative for Asthma, National Heart, Lung, and Blood Institute, 1996. 31 p.

Electronic copies available in English, Arabic, and Spanish in Portable Document Format (PDF) from the Global Initiative for Asthma (GINA) Web site.

Print copies: Available from the National Heart, Lung, and Blood Institute (NHLBI), Information Center, P.O. Box 30105, Bethesda, MD 20824-0105 and the Global Initiative for Asthma Secretariat, Professor Jean Bousquet, Service des Maladies Respiratoires, Hopital Arnaud de Villeneuve, 34295, Montpellier, Cedex 5, France.

Additional, interactive online educational resources are available from the GINA Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on November 4, 1999. The information was verified by the guideline developer as of December 15, 1999. This summary was updated by ECRI on May 22, 2002, April 23, 2004, March 18, 2005, and November 16, 2005.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx.

NGC, AHRQ, and its contractor ECRI make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related

materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 10/9/2006